PREVALENCE OF LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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In partial fulfillment of regulations For award of the degree of

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BONAFIDE CERTIFICATE

This is to certify that dissertation named **"PREVALENCE OF LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE"** is a bonafide work performed by Dr.J.KAMARAJ, post graduate student, Department of Medicine, Kilpauk Medical College, Chennai-10, under my guidance and supervision in fulfillment of regulations of the Tamilnadu Dr. M.G.R Medical University for the award of M.D. Degree Branch I (General Medicine) during the academic period from May 2011to April 2014.

Prof. Dr.N.GUNASEKARAN M.D., DTCD
Director
Institute of Non-Communicable Diseases
SuperintendentGovernment Royapettah Hospital
Government Royapettah Hospital, Chennai-600014.

Prof. Dr.R.SABARATNAVEL M.D.,
Professor and Unit Chief
Department of General Medicine
Professor and HOD
Department of General Medicine
Government Kilpauk Medical College,
Chennai-600010.

Prof. P. RAMAKRISHNAN M.D., D.L.O
The Dean
Government Kilpauk Medical College
Chennai - 600010.

DECLARATION

I solemnly declare that this dissertation **"PREVALENCE OF LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE"** was prepared by me at Government Kilpauk Medical College and Hospital, Chennai, under the guidance and supervision of **Dr.R.SABARATNAVEL M.D.**, Professor, Department of Internal Medicine, Government Royapettah Hospital, Chennai.

This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfillment of the University regulations for the award of the degree of **M.D. Branch I (General Medicine)**.

Place: Chennai

Date: (Dr.J.KAMARAJ)

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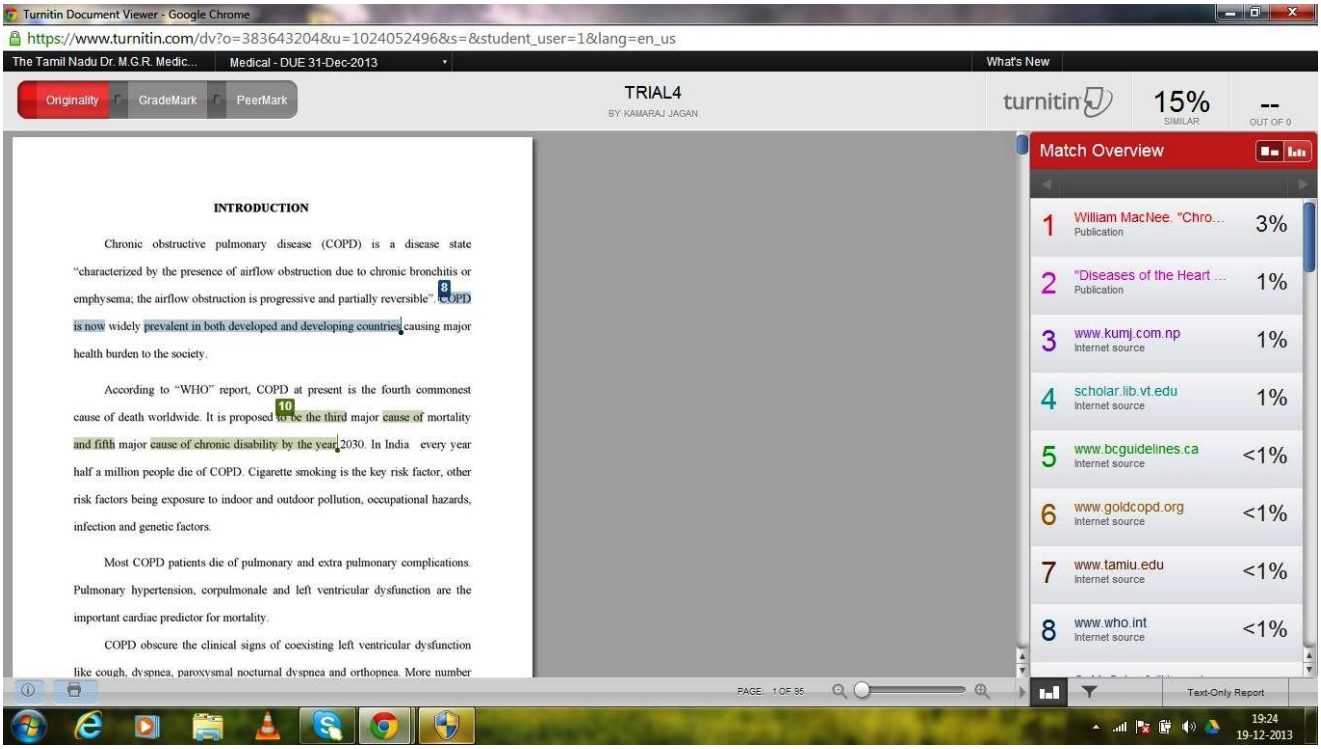
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INTRODUCTION
Chronic obstructive pulmonary disease (COPD) is a disease state "characterized by the presence of airflow obstruction due to chronic bronchitis or emphysema; the airflow obstruction is progressive and partially reversible". COPD is now widely prevalent in both developed and developing countries causing major health burden to the society.
According to "WHO" report, COPD at present is the fourth commonest cause of death worldwide. It is proposed to be the third major cause of mortality and fifth major cause of chronic disability by the year 2030. In India every year half a million people die of COPD. Cigarette smoking is the key risk factor, other risk factors being exposure to indoor and outdoor pollution, occupational hazards, infection and genetic factors.
Most COPD patients die of pulmonary and extra pulmonary complications. Pulmonary hypertension, corpulmonale and left ventricular dysfunction are the important cardiac predictor for mortality.
COPD obscure the clinical signs of coexisting left ventricular dysfunction like cough, dyspnea, paroxysmal nocturnal dyspnea and orthopnea. More number
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INTRODUCTION Chronic obstructive pulmonary disease (COPD) is a disease state “characterized by the presence of airflow obstruction due to chronic bronchitis or emphysema; the airflow obstruction is progressive and partially reversible”. COPD is now widely prevalent in both developed and developing countries causing major health burden to the society. According to “WHO” report, COPD at present is the fourth commonest cause of death worldwide. It is proposed to be the third major cause of mortality and fifth major cause of chronic disability by the year 2030. In India every year half a million people die of COPD. Cigarette smoking is the key risk factor, other risk factors being exposure to...

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ABBREVIATIONS

PROFORMA

MASTER CHART

ETHICAL COMMITTEE APPROVAL CERTIFICATE

PLAGIARISM

PREVALENCE OF LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

ABSTRACT:

Background:

COPD is now more prevalent in both developed and developing countries. It is projected to be the third most common cause of death and fifth most common cause of chronic disability by the year 2030. In India half a million people die of COPD.COPD obscure the clinical signs of coexisting left ventricular dysfunction like cough, dyspnea, paroxysmal nocturnal dyspnea and orthopnea. Symptoms of dyspnea in COPD can be partially due to LV systolic and diastolic dysfunction. More number of patients is either under or wrongly diagnosed, that leads to worsening and development of complications. Early identification and treatment of LV dysfunction can improve the patient's symptoms.

Aim of the study :

To study the prevalence of LV systolic dysfunction in COPD patients and to assess the possible risk factors contributing to the development of LV systolic dysfunction.

Methods and materials:

The study design was approved by the Ethical Committee of the institution. This study was done at Government Royapettah Hospital, Chennai between May 2013 to October 2013 .This is a cross sectional study in which 50 patients with COPD more than 40 years of age. Severity of COPD is assessed by Spirometry. LVEF was measured by 2D Echo. Duration of smoking and smoking index also was calculated.

Results:

Among the 50 COPD patients, duration of smoking, smoking index and severity of COPD correlated with LVEF. . 'p' value was significant. COPD is more prevalent in males. Most patients belong to low socio economic status. COPD severity is directly proportional to smoking index and duration of smoking. Our study reports that 10% of the COPD patients have LV systolic dysfunction. A higher smoking index and prolonged duration of smoking is associated with poor LV systolic function. Increasing severity of COPD is associated with worsening of LV systolic function

Conclusion:

LV systolic dysfunction is directly proportional to severity of COPD. Smoking index and duration of smoking are positively correlated with

development of LVSD. Routine echocardiography is recommended for all severe COPD patients. Smoking cessation should be a vital part of treatment plan in COPD patients. In COPD patients with LVSD, it may be good to introduce selective beta-1 blocker, diuretics, ACE inhibitors, angiotensin-II antagonist and aldosterone antagonist.

Key words:

Chronic obstructive pulmonary disease, smoking, severity of COPD, Spirometry, Echocardiography, LV systolic dysfunction

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a disease state“characterized by thepresence of airflow obstruction due to chronic bronchitis oremphysema; the airflow obstruction is progressive and partially reversible”.COPD is now widely prevalent in both developed and developing countries causing major health burden to the society.

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Most COPDpatients die of pulmonary and extra pulmonary complications.Pulmonary hypertension,corpulmonale and left ventricular dysfunction are the important cardiac predictor for mortality.

COPD obscure the clinical signs of coexisting left ventricular dysfunction like cough,dyspnea, paroxysmal nocturnal dyspnea andorthopnea.More number of patients is either under or wrongly diagnosed,that leads to worsening and development of complications.

Routinespirometeryis used to diagnoseand to assess the severity of COPD and echocardiography is mandatory to assess the cardiac status in COPD patients.

The awareness among patients regarding COPD and its complications is less, so more attention is needed for COPD patients pertaining to the development of complications.

REVIEW OF LITERATURE

HISTORICAL BACKGROUND

COPD has existed since time unknown but has been described by various terminologies in the past. Bonet described a condition named "voluminous lungs" as long back as 1679. In 1769, Giovanni Morgagniproposed lungs becoming "turgid"particularly from some airborne factor.[1]Ruysh provided the first authentic illustration and described the enlarged airspaces in emphysema in 1721.[2]

The destructive nature of the emphysematous lung wasillustrated and described by Matthew Bailliein 1789.[1] In 1814 Badham denoted the word "catarrh" to the cough and mucus hypersecretion in patients with chronic bronchitis and also described it as a disabling state.Rene Laennec, the inventor of stethoscopedescribed “emphysema" in his book as“A Treatise on the Diseases of the Chest and Mediate Auscultation” (1837).

William Briscoe in 1965 designated the term COPD.This terminology has overtaken other lesser popular terminologies and to become the established name for this disease currently. British Thoracic Society(BTS) accepted and adopted the COPD terminology and formulated guidelines for COPD management.

DEFINITION:

American Thoracic Society (ATS) defined COPD is “a disease state characterized by the presence of airflow obstruction due to chronicbronchitis or emphysema; the airflow obstruction is generallyprogressive, may be accompanied by airway hyper-reactivity, and may be partially reversible.”

OTHER NAMES FOR COPD:

Chronic obstructive airway disease (COAD)

Chronic obstructive lung disease (COLD)

Chronic air flow limitation (CAL)

CHRONIC BRONCHITIS:

Chronic bronchitis is defined as “the presence of chronic productive cough for 3 months during each of two successive years in a patient in whom other causes of chronic cough, such as infection with mycobacterium tuberculosis, carcinoma of the lung, bronchiectasis, cystic fibrosis, and chronic congestive heart failure, have been excluded.”

The three forms of chronicbronchitis:

1. Simple bronchitis: mucus hypersecretion.

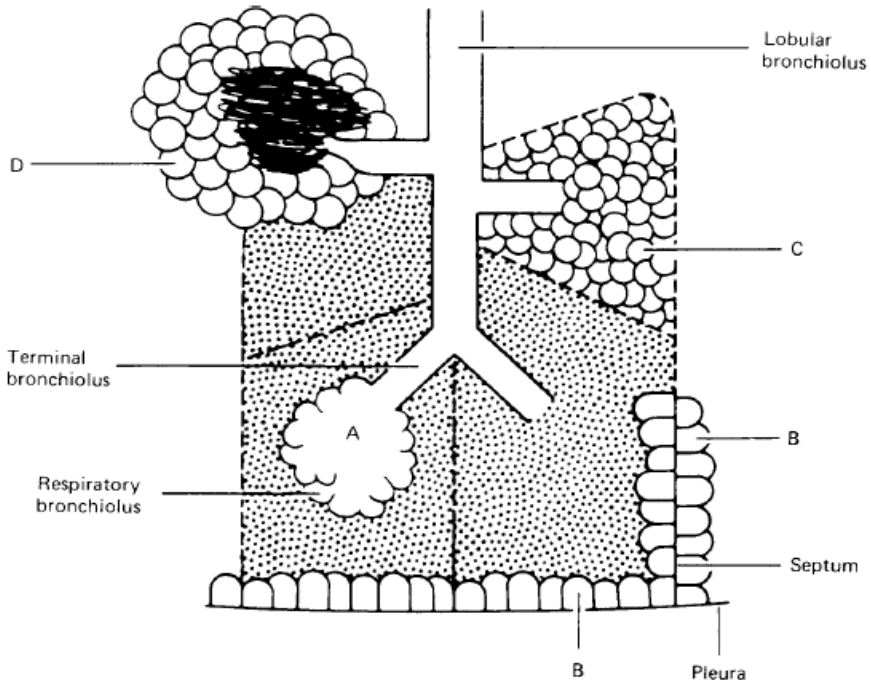
2. Chronic or recurrent mucopurulent bronchitis: intermittent or persistent mucopurulent sputum.

3. Chronic obstructive bronchitis: chronic sputumproductionalongwith airflow obstruction.

EMPHYSEMA:

Emphysema is defined as “a condition of the lung characterized by abnormal permanent enlargement of the air spaces distal to the terminal bronchioles accompanied by destruction of their walls without obvious fibrosis.” “Destruction is defined as nonuniformity in the pattern of respiratory air-space enlargement; the orderly appearance of the acinus and its components is disturbed and may be lost.”

CLASSIFICATION OF EMPHYSEMA



Anatomic varieties of emphysema. *A*. Centriacinar (centrilobular). *B*. Paraseptal (distal acinar). *C*. Panacinar (panlobular). *D*. Irregular (scar). The dashed lines mark the edge of the acinus. Only centriacinar and panacinar emphysema are commonly observed in COPD.

PANACINAR (PANLOBULAR) EMPHYSEMA:

Acini are almostuniformly involved (and lobule).

CENTRIACINAREMPHYSEMA**:**

Dominant involvement of the proximal portion of the acinus (center of the lobule)

PARASEPTAL EMPHYSEMA (DISTAL ACINAR) EMPHYSEMA:

The distal part predominantly involved(alveolar ducts and sacs) and the proximal part relatively spared.

IRREGULAR EMPHYSEMA (PARACICATRICIAL EMPHYSEMA)**:**

Acinus may be irregularly involved, usually associated with obvious scarring.

BURDEN OF COPD

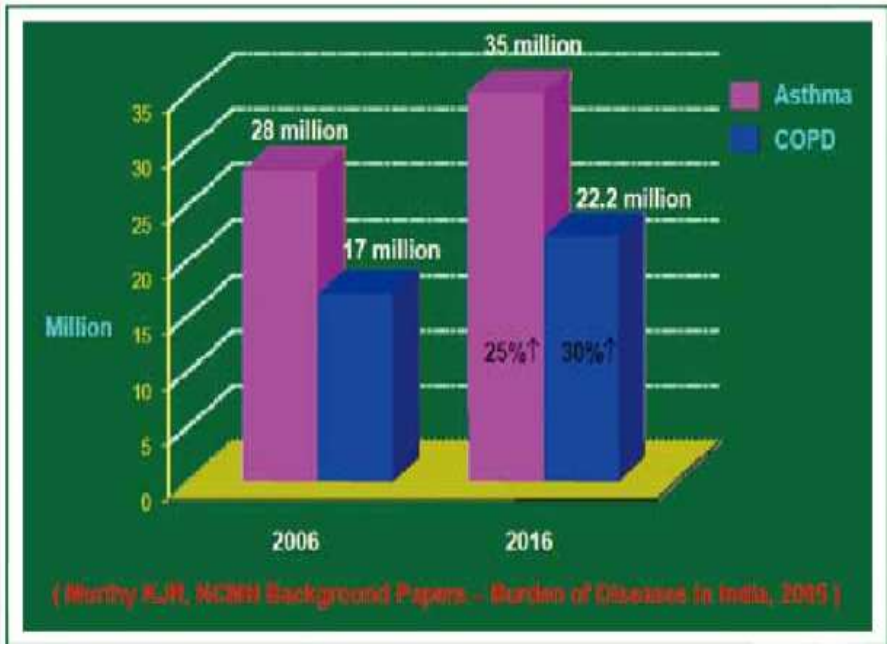
EPIDEMOLOGY

COPD currently tops the list as the major cause of morbidity and mortality throughout the world and contributes significantly to the economic and social burden globally.(4

COPD prevalence,morbidity and mortality directly related to risk factors like smoking, indoor and outdoor pollution.

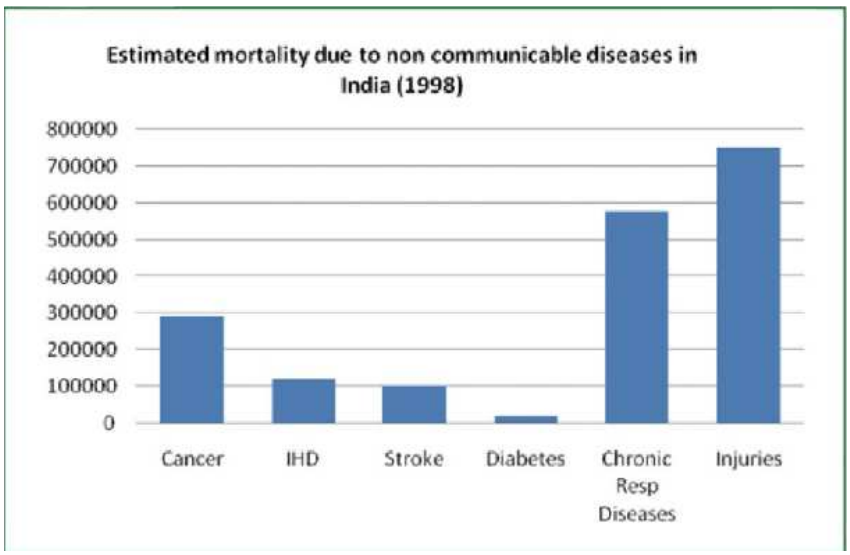
The prevalence is increasing atpresent due to continuous exposure to risk factors.COPD prevalence is more in males than females and with advancing age.Increasing trend in prevalence of COPD is observed among women.Ray et alin

1995found that the prevalence of COPD in male was 4.08 percent and in females was around 2.55 percent from south India.[7] But in SEARO Region higher COPD prevalence was observed among women than men due to indoor air pollution (Pandy 1984; Behera and Jindal 1991).[9] National health interview surveyreport in United States in the year 2007 to 2009 shows the COPD prevalence was higher in older age groups, and most of the lifespan women had higher rates than men.NCMH estimates in India there were around 17 million COPD patients in 2006 but it is around 22 million in the next 10 year.[11]



Acute exacerbation of COPD is a greatest burden. In European countries direct cost of respiratory disease is 6% of total health budget, with COPD accounting 56% of this cost of respiratory disease[8].

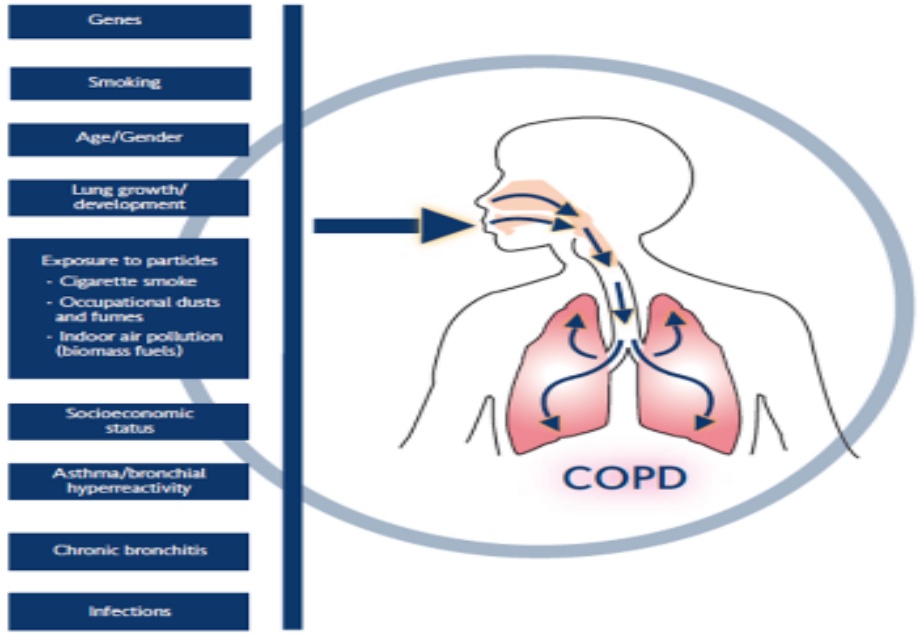
COPD kills more than 3 million people every year worldwide.[5]At present it is the fourth leading cause of death, by the year 2030 it becomes third leading causeof death..In India half a million people die of COPD. [6]This is4 times the mortality that it causes in USA and Europe.[122]Nongkinryhet al published the WHO data of non-Communicable disease in India from 1998 to 2002 (JAPI, 2004). Asthma and COPD were second most cause for mortality. The morbidity figures around 55million cases for both Asthma and COPD.[12]



COPD mortality increases with age and the incidence is higher in men than women.[13,14,15,]Theincomplete recognition and diagnosis of COPD further miscalculates the prevalence, morbidity and mortality rates. Most COPD patients do not die of the disease per se andalsodue to accompanyingco-morbid conditions.[16]

ETIOLOGY OF COPD:

COPD is a major health problem principally in societies where cigarette smoking is common and nonsmokers also develops the disease.



Risk factors for the development of COPD may be broadly divided into those related to environmental exposure and host factors.

Risk Factors for COPD	
Environmental	**Host-based**
Smoking	Genetic factors
Occupational exposures	Asthma/airway hyperreactivity
Air pollution	
Childhood respiratory infections	
Low socioeconomic status	

Smoking is the major risk factor; other risk factors are alpha 1-antitrypsin (α1-AT) deficiency, occupational exposure, childhood lower respiratoryinfections, airway hyper responsiveness, geneticfactors and low socioeconomic status.In

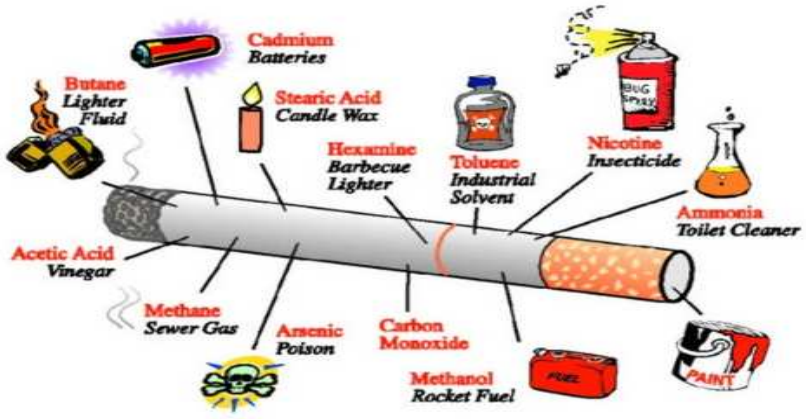
alpha1-antitrypsin deficiencysmoking exacerbatesthedevelopment ofemphysema indicating a clear genetic predisposition to COPD. [17]In India biomass smoke exposure becomesa major risk factor andburning of mosquito coils also a common indoor air pollutant.

ENVIRONMENTAL

SMOKING

In the United States therisk of developing COPD due to tobacco smoking accounts for 80% to 90%. [19] FEV1 begins to decline at 30–35 years of age in non-smokers but in smokers this may occur earlier.[22]Nonsmokers commonly have decline the rate FEV1 of about 30mL .Smokers on the other hand have a decline inFEV1 of about 50 ml. In males, the loss of FEV1 in excess of the normal decline with aging is 9 ml per year for each pack-year of smoking;in females, the excess rate of decline is 6 ml.The risk of developing COPD isgreater in tobacco exposures.[20] Swedish cohort study concluded that smoking was a causative risk factor of COPD and the attributed risk in a given population was 76.2 %[27] where as In Denmark study itwas 74.6 percent.[28]BTS guidelines reported that most COPD patients have history of at least 20 pack-year of smoking.[21]Cigarette smokers have a higher prevalence of chronic bronchitis. Confounding factors like inhaled cigarette smoke, tar, nicotine and other constituents may complicate the

relationship between the numbers of cigarettes smoked andrate of decline in FEV1.[23]



Cigarette smokers had a significantly higher mortality rate compared to nonsmokers. Cessation of smoking does not substantially improvethe FEV1 but the subsequent rate of disease progression is decreased. [24,25] Indian people smoke tobaccoin various forms like beedis, hookahs and chillums. The chillum is the most harmful of the lot followed by hookahs and beedis respectively. Beedis are moredangerous than cigarettes (it contains only one fourth the amount of nicotine, but it produces four to five times more tar than cigarettes).(26)

OCCUPATIONAL EXPOSURE:

The effect of occupational exposures is usually small compared to cigarette smoking, but increased risk for accelerated loss of lung function.(38)Agricultural and dusty occupations are augments the risk of developing chronic bronchitis by two- to threefold and with smoking combination the risk increases to sixfold.(32,33)

Several specific occupational exposures including coal mining, gold mining,cotton textile dust, welding, construction, plastic manufacturing and utility all have been suggested as risk factors for chronic airflow obstruction. The high prevalence of smoking among workers in certain occupation has been a major confounding factor. Occupational exposures to organic and inorganic gases and fumes also lead to higher vulnerability to COPD. Workers exposed to cadmium can develop emphysema. [39]

OUTDOOR AIR POLLUTION:

This public health problem occurs mainly from the emission ofpollutants from motor vehiclesandindustries.(29)Particulate pollutants, ozone, nitrogen dioxide and sulphur-dioxide areproduce airway oxidative stress, bronchial hyper reactivity, systemic as well as pulmonary inflammation, reduction in airway mucosal cilliary activity and amplification of viral infections.(30) In community-based study,higher traffic density wasassociated withdiminished FEV1 and
FVC.(31)In low-income countries outdoor air pollutant levels tend to be higher.

INDOOR AIR POLLUTION:

Commonly theindoor air pollutants are environmental tobacco smoke,particulatematter, carbon monoxide (CO), NO_2, volatile organic compounds andbiological allergens.The major indoor air pollutants that are related to the development of COPD are tobacco smoke and biomass exposure.(34)The

contributing factors for indoor air pollution are wood, animal dung,crop residues and coal are burned in open fires and poorly functioning stoves in poorly ventilated indoors are the contributing factors for indoor air pollution. Women's are spending more time in indoors for cooking than men, andexposed to biomass fuel combustion products, so theyare prone to develop COPD.[36,37] In India exposure to biomass smoke is a major one and burning of mosquito coils at homes are common indoor pollutants for the genesis of COPD. Burning one mosquito coil is equivalent to around 100 cigarettes because it emits as much particulate matter pollution.[35]

LOWER RESPIRATORY TRACT INFECTIONS:

Previous tuberculosis, childhood asthma and respiratory infections are the risk factors to develop COPD.Childhoodlower respiratory tract infections might produce permanent damage or impair growth and development of the lung. In Lung Health Study COPD exacerbations in smokers were associated with an additional loss of FEV1 of 7 ml per year for those having one exacerbation per year.

LOW SOCIOECONOMIC STATUS:

COPD incidence, prevalence, morbidity and mortality rates are inversely relatedtosocioeconomic status. Poor housing condition, overcrowding, poor environment, poor nutrition, alcohol, tuberculosis and recurrent lower respiratory infections are the common risk factors in low socioeconomic status people.

HOST FACTORS:

GENETIC FACTORS:

The association between the development of early-onsetemphysema and alpha1- antitrypsin deficiency was first described by Eriksson in 1963. [(40)]In alpha1-AT deficiency premature development of pan lobular emphysema and early decline in lung function occurs. M allele is fornormal alpha1 antitrypsin.Mutation in the SERPINA1 gene [located on the long arm of chromosome 14 (14q31-32.3)] and forms the Z allele results severe alpha1-antitrypsin deficiency[(41)].In COPD variety of genes including beta1microsomal epoxide hydroxylase-1,tumor necrosis factor alpha and transforming growth factor are associated for pathogenesis.

ATOPY AND AIRWAY HYPERRESPONSIVENESS:

Dutch workers in the 1960s proposed that smokers with COPD and asthmatics shared common characters like airway hyper responsiveness, allergy and eosinophilia.[(42)] Atopic individuals have high serum IgE and eosinophil levels.

The probable mechanisms for increased AHR in smokers with COPD:

1. Shortening of the airway smooth muscle and increased thickening of the airway wall.
2. Inhaled aerosolsdeposition is in the centrally that result of airways obstruction,
3. In emphysema alveolar wall loss results in loss of airway wall support.

4.Airway wall edema is due toincreased permeability of airway epithelium.

ASTHMA:

Childhood asthma,chronic untreated and partially treated asthma can progress to fixed airflow obstruction. Tucson epidemiological studies had showed that asthmatics have a twelvefold increase risk of develops COPD than non-asthmatics.

PATHOGENESIS:

The probable pathogenesis of COPD is proteinase-antiproteinase hypothesis, immunological, imbalance of oxidant-antioxidant,apoptosis,systemic inflammation, and ineffective repair.[44]

PROTEINASE-ANTIPROTEINASE HYPOTHESIS

In healthy lungs damage does not occur because the release of proteolytic enzymes from inflammatory cells inactivated by inhibitors. In condition of excessive enzyme load or where there is functional or absolute deficiency of antiproteinase, an imbalance develops between proteinases and antiproteinase.

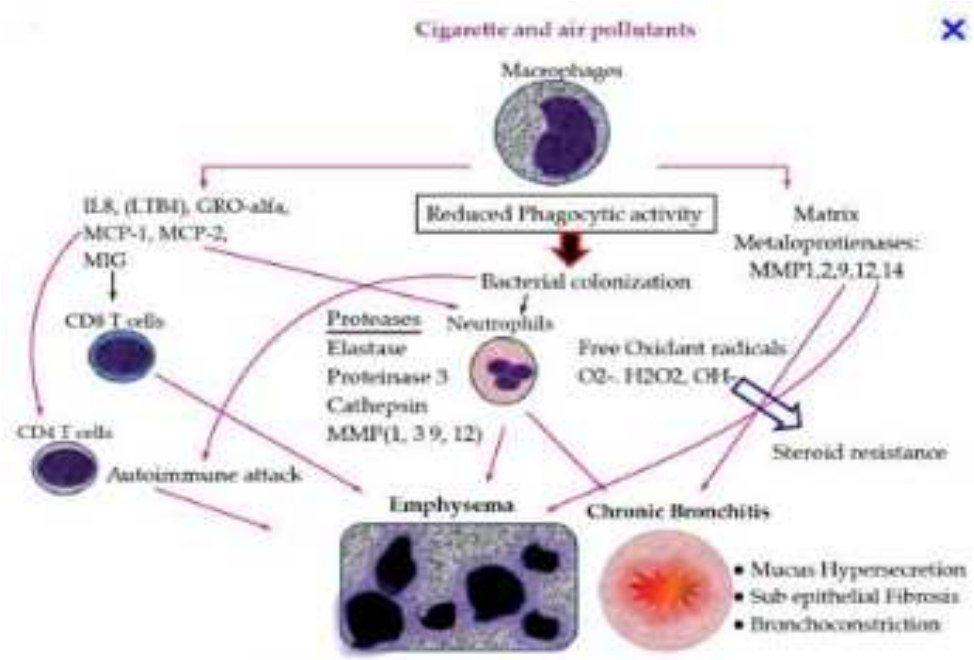


Fig. 1 ıogenesis of COPD

This leads to degradation ofconnective tissue in alveolar wall and development of emphysema. Cigarette smoke stimulate the airway epithelium and to trigger the airway remodeling. [(46)] In chronic smokers haveaccumulation of neutrophils, activated macrophages and CD8+ T lymphocytes in the distal airways and alveolar spaces.[(45)]The activated neutrophils produce moreneutrophil elastase.Matrix metalloproteinase (MMP) activity is increased in COPD.MMP-2, 9 and 12 are increased in smoking associated emphysema. Other proteases that play a role in the COPD pathogenesis are cathapsins S, L, G and proteinase-3.[(47)]MMP andneutrophil elastase degrades the elastin fragments of the alveolar wall and leads to thedevelopment of emphysema.

IMMUNOLOGICAL MECHANISM:

COPD patients have more numbers of neutrophils in sputum and lung tissue. In smoking-induced COPD immunoglobulin free light chains and IgE levels are increased.[48,49]

OXIDANT AND ANTIOXIDANT BALANCE:

Reactive oxygen species (ROS) in cigarette smoke or released by inflammatory cells and structural cells of the lungs in response to smoke may lead to lung injury.In smokers there isincreased theROS (hydrogen peroxide, hydroxyl radicals, superoxide radicals, H_2O_2, and 8-isoprostane)and decreased plasma antioxidantsproducts such as 4-hydroxynonenal, 3-nitrotyrosine. Oxidative attack may inactivate antiproteases. Due to decreased production of inactivated histone deacetylases oxidative damage occurs and this leads to a prolonged inflammatory response.Vasodilation and endothelial cell growth impairs in Oxidative stress. Oxidants modify the elastin and the modified elastin is more susceptible to proteolysis. Oxidant augments matrix degrading capacity which can promote emphysema.[50]

INFLAMMATION

Smoking and inhaled irritants lead to recruitment of inflammatorycells in the lungs and airways.These recruited cellproducts injure the lung tissue and disrupt the

normalmechanisms of repair. In COPD neutrophils, eosinophil's, macrophages, and lymphocytes are associated for inflammation. Interleukin-8 (IL-8), macrophage inflammatoryprotein-1α (MIP-1α), and monocyte chemo-attractant protein-1(MCP-1) are up-regulated in bronchiolar epithelium in COPD. CD4+ and CD8+ T cells and B cells accumulate in alveolar and airway tissue in COPD. Among these cells CD4+ are predominantly elevated.

SYSTEMIC INFLAMMATION:

Pro-inflammatory cytokines andchemokine's are released into the circulation as a result of persistent pulmonary inflammation.[51] These mediators stimulate bone marrow,liver and adipose tissue to release excessive amounts of leucocytes, IL-6, IL-8,C-reactive protein (CRP), fibrinogen and tumor necrosis factor-α (TNF-α) into the circulation.[52,53] Systemic inflammation may initiate or worsen the comorbid illness, such as normocytic anemia,IHD, Cardiac failure,osteoporosis, cancer lung, diabetes and depression.

APOPTOSIS:

InCOPD patients lung apoptotic alveolar endothelial and epithelial are increases.Mediators involved in apoptosis are,vascular endothelial growth factor, caspase-3 and ceramide.

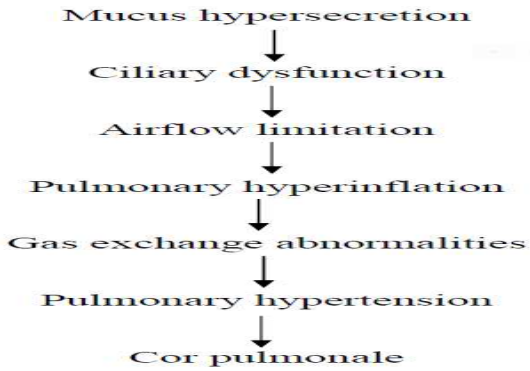
INEFFECTIVE REPAIR:

The repair in emphysema not effective is due to the damaged alveoli have limited ability is to repair.

PATHOPHYSIOLOGY

In COPD Pathophysiological changes occurs in central airways, peripheral airways, paranchyma of the lung and pulmonary vasculature. The defining physiological feature ismaximal forced expiratory flow reduction is persistent. The typical features areincreased theairway resistance, increased theresidual volume, increased the residual volume/total lung capacity ratio,decreased the inspiratory capacity, maldistribution of ventilation, and mismatching of ventilation-perfusion.Loss of lung elasticity, increasedairways resistanceand decreased lungcompliance are the factors that reduce forced expiratory flow.

Pathophysiological changes occur in the following order in COPD.



MUCUS HYPER SECRETION:

In COPD patients with predominant central airway involvement the common featutre is mucus hypersecretion.It is due to enlargement submucus glands and metaplasia with increased numbers of globet cell in chronic irritation of the respiratory epithelium.

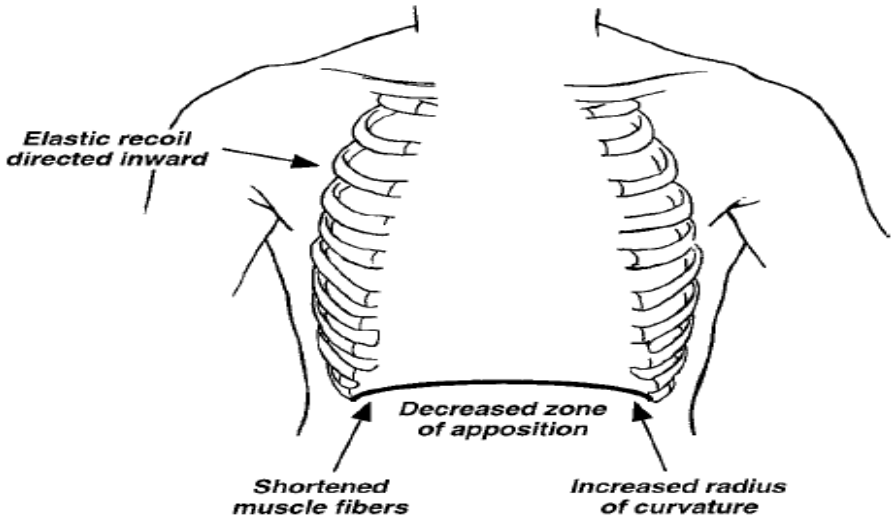
AIR FLOW LIMITATION:

The characteristic feature of COPD patient is decrease in FEV_1 and FEV_1/FVCratio probably due to inflammation, fibrosis and luminal exudates

in small airways.(54)

HYPERINFLATION:

It is described by decreased inspiratory capacity and increase in functional residual capacity. Hyperinflationproduces the following effects.



(1) Decreases the zone of apposition between the diaphragm and the abdominal wall, rib cage movement are hindering.

(2) Diaphragmatic muscle fiber length shortens, decreasing the force that can be generated by the diaphragm.

(3) The radius of curvature of the diaphragm increases and decreasing transpulmonary pressure (at constant tension).

(4) Diaphragmatic muscle fibers medially directs and impairing inflation with diaphragmatic contraction.

PULMONARY GAS EXCHANGE ABNORMALITIES

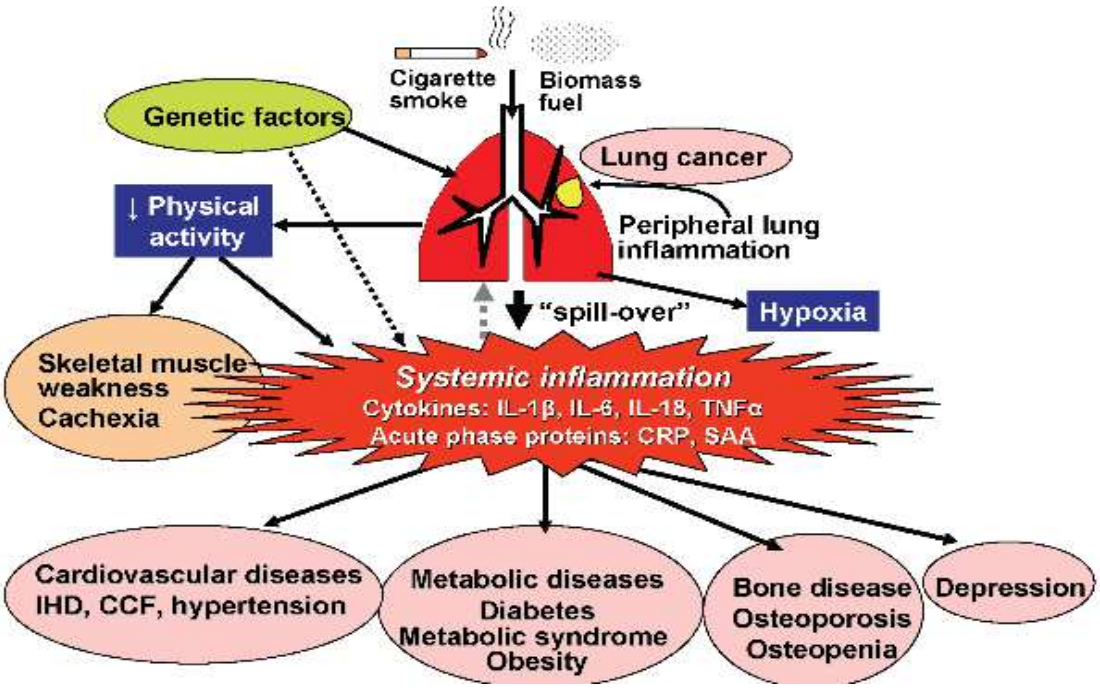
In COPD Ventilation–perfusion ($\dot{V}$a/$\dot{Q}$) mismatching is the most vital cause of decreased pulmonary gas exchange. Other less importantcauses are alveolar hypoventilation, impaired alveolar–capillary oxygen diffusion and increased shunt. In COPD patient'sventilation distribution is unequal. As a result of emphysema reduction in blood flow due to local destruction of alveolar vessels, hypoxic vasoconstriction in alveolar hypoxemic areas and passive vascular obstruction as a result of increased alveolar distension and pressure.This results in hypoxemia and hypercapnea.

PULMONARY HYPERTENSION:

In patients with long term COPD the development of pulmonary hypertension is due to hypoxic vasoconstriction of pulmonary

arteries.Progressivepulmonary hypertension leads to the development ofventricular hypertrophy and corpulmonale.

SYSTEMIC FEATURES:



COPD with smoking history have the higher comorbidities was observed in the ECLIPSE study.[62] The following comorbidities associated with COPD are cardiovascular disorders (Hypertension, CAD and Chronic cardiac failure), metabolic diseases (metabolic syndrome, obesity and diabetes), bone disease (osteopenia and osteoporosis), skeletal muscle weakness, anemia, stroke, lung cancer, cachexia, depression and cognitive decline.[63]

Cachexia is a common feature of severe COPD.The probablemechanism of cachexia is low testosterone levels, increased catecholamine synthesis and

increased levels of pro-inflammatory cytokines. [55,56,57] The fat-free mass is significantly reduced in COPD.[58]There may be weakness and loss of skeletal muscle mass due toincreased apoptosis and disuse of the muscle. Usually the skeletal muscle mass loss is seen in thighs and upper arms.[59]The dysfunction of theskeletal muscle is exaggerated by poor nutrition, hormonal changes and use of corticosteroids.[61]The skeletal muscle dysfunction results in reduced exercise intolerance and with symptoms of fatigue and dyspnea.[60]In patients with severe COPD the factors contribute to the generalized muscle weakness are hypercapnia, hypoxemia, infection, electrolyte and mineral deficiencies.In spite of a normal or increased dietary intake weight loss is more common in severe COPD. Systemic inflammation, increased oxidative stress, increased thrombotic tendency and neuro-humoral disturbances are the risk factors leading to the development of cardiovascular disease in COPD patients. [64] The osteoporosis risk increases by 1.9-fold in COPD patients and by 2.4-fold in severe COPD patients.[65] The probable etiology for the bone loss are smoking, sedentary lifestyle, low body mass index, vitamin D deficiency, hypogonadism, and use of glucocorticoids.[66]COPD patients are more vulnerable to develop fractures particularly vertebral fractures. In COPD patient's risk of lung cancer is high in smokers than nonsmokers.In COPDpatient'sprevalence of depression is higher in females, current smokers, and

severe disease.[67, 68] Anemia is common than polycythemia and it reduce the functional capacity.

CARDIO VASCULAR CHANGES:

Pulmonary hypertension and corpulmonaleare the consequence of chronic alveolar hypoxia; the secondary contributions are from destructionof the alveolar capillary bed, lung hyperinflation and increased blood viscosity.The chronic alveolar hypoxia produces a characteristic remodeling of the pulmonary arteries. The three major components remodeling are. 1. Extension of the medial muscle into the pulmonary arterioles.[69,70] 2.Proliferation of muscle that becomes progressively thickens and occludes the vascular lumen. Insevere cases Intimal fibrosis may occur. 3. Inner muscular tube develops in the smallpulmonary arteries.[71] In the late course of COPD hypoxemia and hypercapnia leads to pulmonary arterial hypertension.

The followingpulmonary vasculature changes occur in the pulmonary vascular bed in COPD patients.

1. Intimal thickening of the small pulmonary arteries is the earliest change.It is due to worsening of the airflow limitation.[72,73]
2. Medial hypertrophy of the muscular pulmonary arteries.[74]

   In patients with COPD pulmonary arterial thrombosis maybe due to Peripheral airwayinflammation.[75]

In COPD patients the following factors contribute to develop of pulmonary arterial hypertension:

1. Pulmonary vascular bed destruction

2. Blood gas tensions abnormality

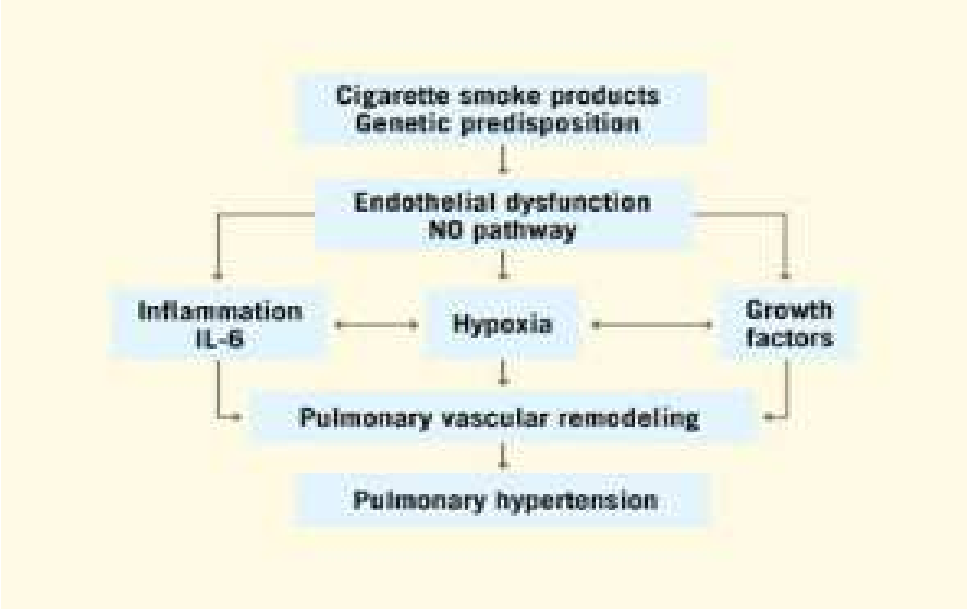
3. Pulmonary mechanics abnormality

4.Increased Cardiac output

5. Alteration in blood volume

6. Blood velocity Increased

7. Abnormal endothelium



Classically, pulmonary hypertension in emphysema has been attributed to the following factors:

1.Hypoxia leading to vasoconstriction and vascular remodeling

2. Hyperinflation compressesthe alveolar vessels and pulmonary vasculatureby physical obliteration.

3. Other possible influences include elevated end-expiratory intrathoracic pressure due to dynamic or static hyperinflation or use of expiratory muscles.[77]In smokers theproduct of tobacco produces inflammatory changes and pulmonary vascular remodeling.[82]The imbalance between vasoactive constrictor and dilator substances produce pulmonary hypertension.Nitric oxideinhibits cell proliferationinthe pulmonary vasculature and prevents vascularremodeling. In COPD patients with hypoxemia there is a reduction in nitric oxide levels and development of pulmonary hypertension. [76]Oswald-Mammoser and colleagues observation had shown that the worsening of pulmonary hypertension is directly associated with severity of airflow obstruction.[80,81] Burrows and coworkers found that emphysematous patients had higher pulmonary vascular resistance andlower cardiac output.[79]

Corpulmonale was defined by a WHO expert committee as “hypertrophy of the right ventricle resulting from diseases affecting the function and structure of the lungs, except when these pulmonary alterations are the result of diseases that

primarily affect the left side of the heart". COPD patients have a highpulmonary vascular resistance as a result ofhypoxia.This causesincreased workload on the right ventricle leading toright ventricular hypertrophy(RVH), right ventricular dilatation and right heart failure.[77]In COPD patients the earliest sign of RV pressure overload is concentric right ventricular hypertrophy. The capacity of the RV to adapt to a high after load is overwhelmed duringacute exacerbations,overwhelmhence precipitating RV failure.[82]

In RV dilation there will be an increase in end-diastolic volume that shifts the inter-ventricular septum into the left ventricle to reduce LVend-diastolic volume and diastolic compliance.[82]In COPD large intra-thoracic pressure changes and long standing RV pressure overload can produce RV hypertrophy and dilatation that shift the inter-ventricular septum into LV cavity during systole and results in the limitation of left ventricular cavity dimensions, contractility, compliance, and rise of the left ventricular diastolic pressure[88,89,90,91]and alteration of LV systolic function.[84,85,86,87]

In pulmonary hypertension blood flow through bronchial circulation increasesand produces right-to-left shunt, resulting in significant amount of desaturation of left atrial blood that contributes to the progressive hypoxia. The myocardial contractility is decreased due todecreasedarterial oxygen tension.[94,95,97]

In Hypoxia the accumulation of excess toxic metabolic products like K^+, H^+ and lactic acidin the cardiac tissue impair the myocardial contractility producing diminished LVEF[88].

Endothelial surface enzymes control the level of circulating compound such as bradykinin, serotonin, angiotensin and adenine nucleotides. During hypoxia there is endothelial dysfunction and altered enzyme activity may lead to atherosclerosis and ischemia of cardiac muscles.[96]

Hyperinflation, increased work of breathing, and raised intra-thoracic pressures also have an impact on the LV functioning.

Sabit et al. had shown that the subclinical COPD have right ventricular dysfunction may be related to airways obstruction and left ventricular dysfunctionrelated to stiffness of the arteries. RV dysfunction is due to raised pulmonary arterial pressure and LV dysfunction is associated with increases afterload due to increased aortic stiffness.[93]

Mechanisms of impaired LV filling in very severe COPD include alveolar hypoxia and pulmonary vascular changes, hyperinflation of the pulmonary system, and ventricular interdependence.In very severeCOPD hyperinflation can cause increase intra-thoracic pressure that exceedpulmonary venous pressure and leads to reductions in blood volumes of both ventricles.

The following are also the mechanisms of heart failure.

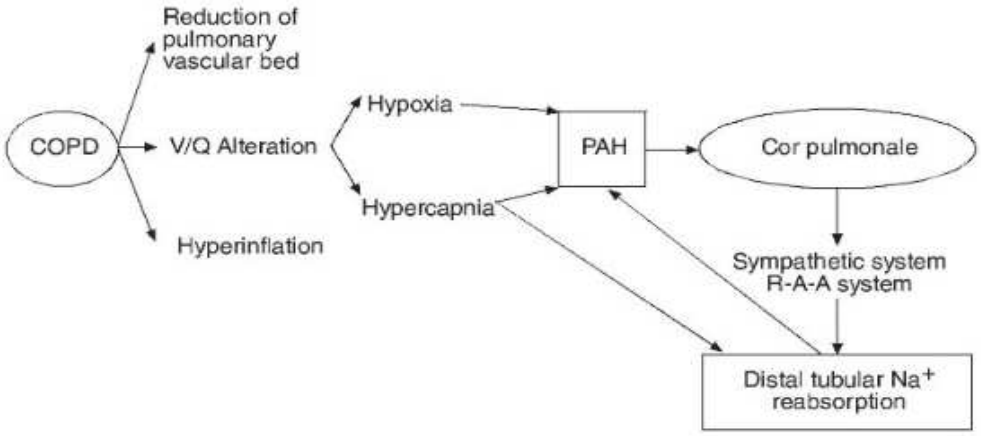
1. Renin-angiotensin aldosterone system activation.
2. Sympathetic nervous system activation andvasopressin.
3. Generation of pro-inflammatorycytokines.

The above mentioned mechanisms are responsible for increasingvascularresistance, increasing heart rate, worsening myocardial perfusion, alteringrenal blood flowandatrialfibrillations.Ischemia and arrhythmias are worsening the LVdysfunction and precipitating cardiac failure.[83] Skeletal muscle alterations increase the LV strain and dysfunction under the conditions of stress. Acute infections, severe anemia,hypertensive emergencies, cardiac arrhythmias (MAT, AF), ischemia, pulmonary embolism and cardio toxicdrugs may precipitate HF in COPD patients.

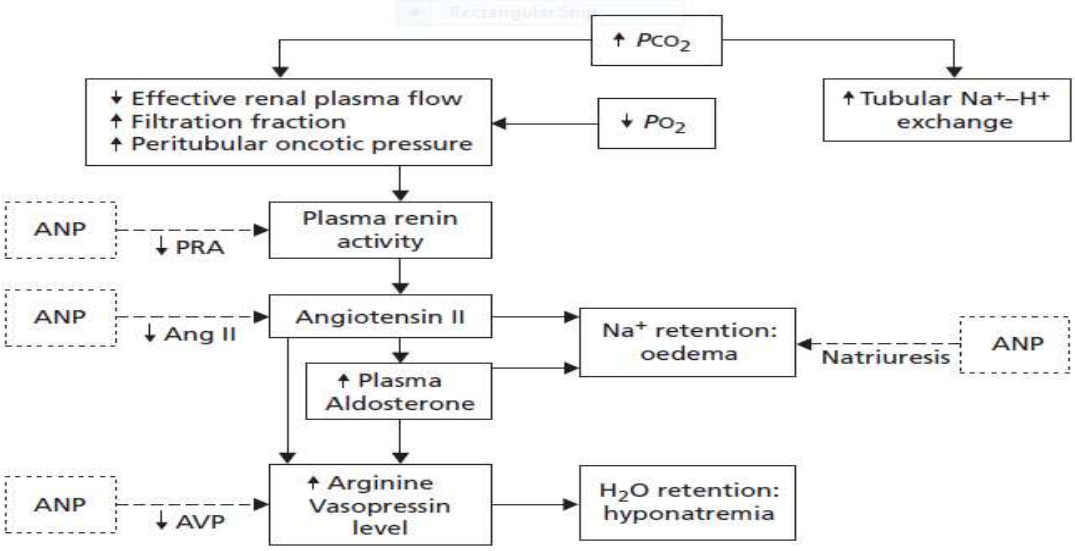
SUPRAVENTRICULAR ARRHYTHMIAS:

Supraventricular tachyarrhythmiasare common in patients with COPD, as a consequence of right atrial enlargement,increased adrenergic tone, hypoxemia and treatment with theophylline,anticholinergics and bronchodilators.

EDEMA:



COPD patient'salterations in salt and water balance are due to hypoxia and hypercapnia. The activation of renin–angiotensin system bydiminution of renal blood flow andraise in AVP as a result of alteration in the blood gases concentration.

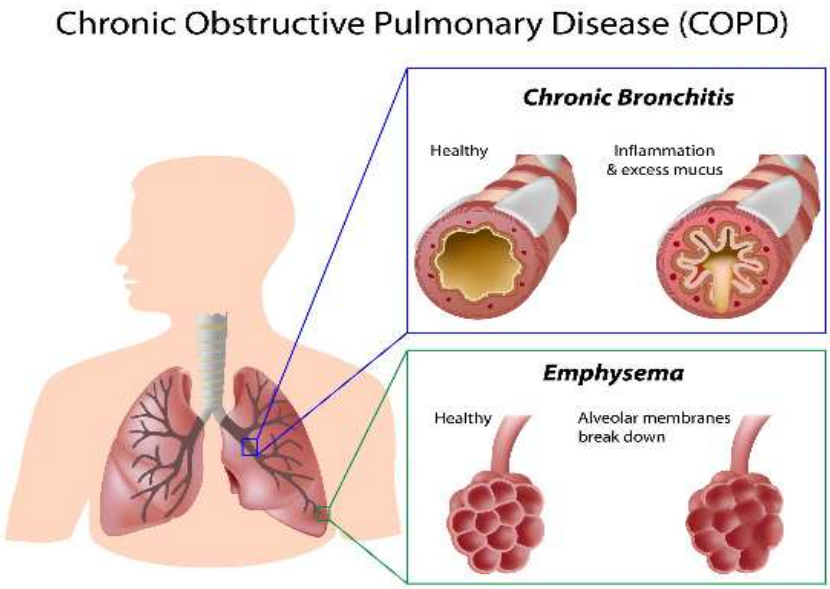


Hypercapnia increases the catecholamine release via a neural mediated action and reduces the renal blood flow. In pulmonary hypertension increase the release of

ANP is due to increases theatrial stretch.[98]ANPhas important beneficial effectsthat could act to prevent the formation of edema in patients with COPD, including the promotion ofnatriuresis,[99]decreasesplasma renin activity, decreases angiotensin II andaldosterone production. [100]Therenin–angiotensin system activation overwhelms the protective mechanisms and leading to develops edema.

PATHOLOGY:

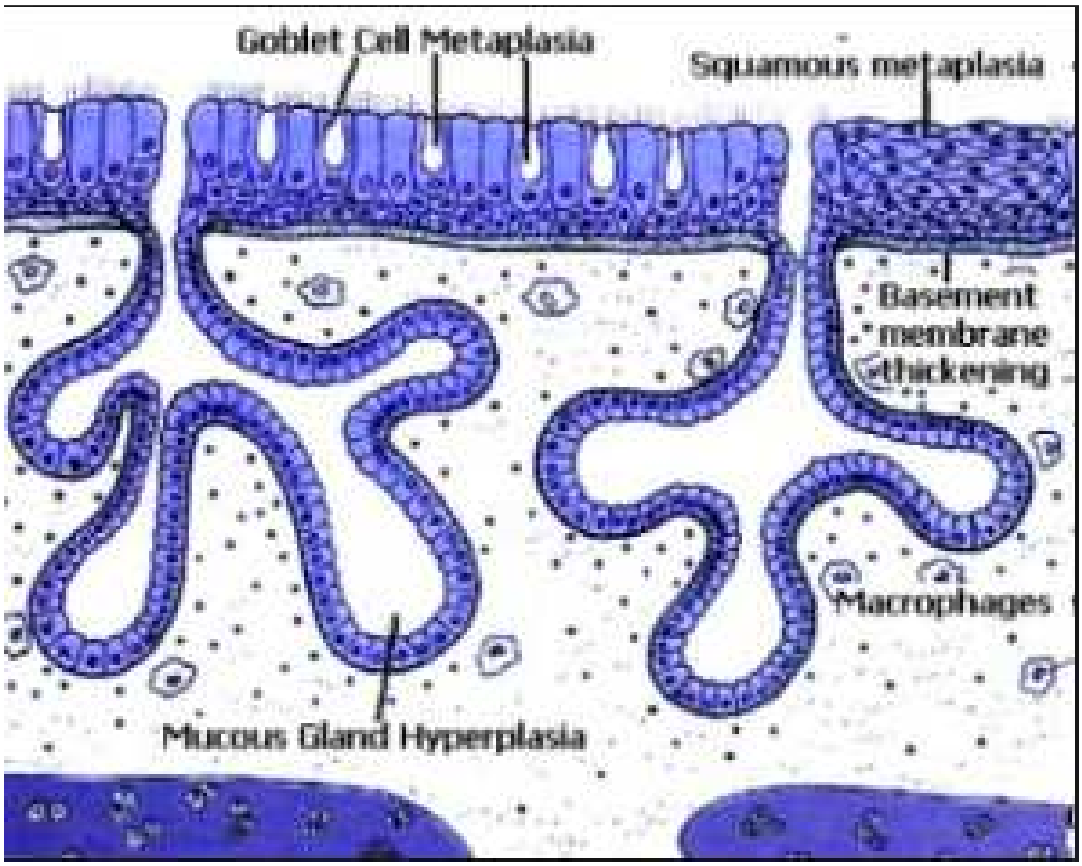
In COPD patients the pathological changes occurs in the large and small airways and alveoli.



Large airways:(Central airway-bronchi>2mm internal diameter):

In chronic bronchitis, goblet cells become hyperplastic and the mucus glands are

enlarged.In smokers goblet cells increase innumber and extend to more peripherally.Bronchi also undergo squamous metaplasia.[52]



Reid index quantifies thehypertrophy of the mucous gland.“Reid index is the ratio of the distance between the basement membrane of the airway epithelium and the cartilage to the thickness of the gland layer”, Normal ratio is 3:1. In normal individuals, it is 0.44+0.09.In chronic bronchitis, it is 0.52+0.08.If the sub mucosal layer thickness is >50% of bronchial wall thickness it is highly suggestive of chronic bronchitis.

Small airways(peripheral airways-bronchiole <2mm internal diameter):

Narrowing and destruction of terminal bronchioles are characteristic changes in COPD. Airway inflammation andscarring of thesmaller airways are associated with airways obstruction.

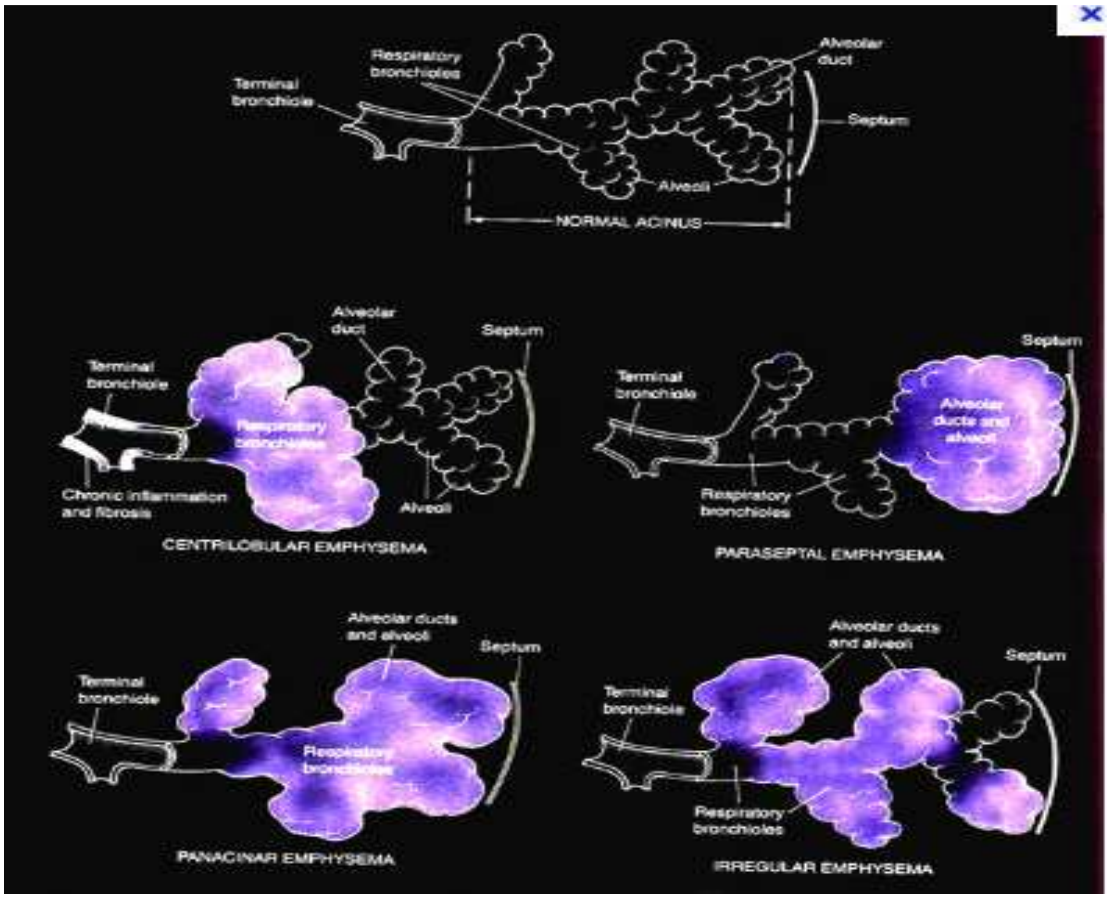
In COPD the following cellular events that occur in the small airways:

1. Mucus secreting cells replaced by Clara cells
2. Mononuclear cellinfiltration
3. Goblet cell metaplasia.[50]

Theimportant finding is Smooth muscle hypertrophy .Thecauses of airway narrowingare excessive secretion of mucus, formation of edema, cellular infiltration and fibrosis.[52]

Lung parenchyma(respiratory bronchioles andalveoli):

Emphysema were first described by Laennec[101] and defined as"dilatation and destruction of lung tissue beyond the terminal bronchiole".[102,103]Emphysema is described bydestruction of gas-exchanging air spaces.According to the distribution of enlarged airspaces within the acinar unit emphysema types described.



Centriacinar (syn. Centrilobular) emphysema:

This kind of emphysemais associated with tobacco smoking. The enlarged airspaces are clustered around the terminal bronchiole. It ismore common in upper and lower lobes of the upper zones.

Panacinar (syn. pan lobular) emphysema:

The enlarged airspaces are dispersed throughout the acinar unit .It is associated with α1-AT deficiency and found anywherein the lungs but more marked at the bases.

Periacinar (syn.Paraseptal or distalacinar) emphysema:

The enlarged airspaces are along the edges of the acinar unit, where it is abuttingthe pleuraor vessel.

Scar or irregular emphysema:

It is described as enlarged airspaces around the scar margins that are notrelated to the structure of the acinus.

CLINICAL FEATURES:

Symptoms:

Cough with or without expectoration.

Breathlessness

Chest pain- may be related to intercostal muscle ischemia.

Haemoptysis

Weight loss, Effort intolerance,Ankle edema.

Signs:

- Nicotine staining of fingers and teeth.

- Nonspecific features of over inflation of the lungs with horizontal ribs, splaying of lower costal margin &widened xiphisternal angle.

-Paradoxical inward movement of lower ribs (Hoover's sign).

- Cardiac dullness reduced.

- Intensity of breath sounds reduced.

- Crepitation's, Expiratory wheezes.

-Pursed lip breathing.

-RVH heave palpable in the subcostal angle or at lower sternal edge, loud P_2.

- Third sound audible in the left fourth intercostal space, Pan-systolic murmur at the left sternal edge, Right ventricular gallop rhythm, elevated jugular venous pressure, pedal edema and tender hepatomegaly in corpulmonale.

	Predominant bronchitis	**Predominant Emphysema**
General Appearance	Mesomorphic; overweight, dusky with suffused conjunctivae, warm extremities	Thin, often emaciated, pursed lip breathing, anxious, normal or cool extremities
Age, years	40 to 55 years	50 to 75 years
Onset	Cough	Dyspnea
Cyanosis	Marked	Slight to none
Cough	More evident than dyspnea	Less evident than dyspnea
Sputum	Copious	Scanty

Upper respiratory Infections	Common	Occasional
Breath sounds	Moderately diminished	Markedly diminished
Corpulmonale	Common	Only bouts of RTI and also terminally
Radiography	Normal diaphragmatic position; cardiomegaly; lungs normal or having increased bronchovascular markings	Small tubular heart; low flat diaphragm; Area of increased radiolucency
Other names	Blue bloater	Pink puffer

Blue bloaters:

Development ofhypoxemia, hypercapnia polycythemia and edema occurs relatively early in blue bloaters..

Pink puffer:

Pink puffers are thin,dyspneicandpreserve blood gas values until late in the course of the disease and develop pulmonary hypertension inadvanced disease state.

INVESTIGATIONS:

SPIROMETRY:

Spirometry is asound test of airflow limitation in patients with COPD. It is the goldstandard test for diagnosis and monitoring its progression. Normal curve has a brisk flow near total lung capacity, then a steady decline down to residual volume. Inspiratory limb is a smooth semicircle. With the development of disease in small airways the expiratory limb begins to dip at lower volumes. Spirometry measures the forced vital capacity (FVC),forced expiratory volume in one second(FEV_1) and ratio of the two measurements(FEV_1 /FVC).A low FEV1 and FEV1/ FVC ratio below the normal range is the diagnostic criteria for COPD.[104-106]A post bronchodilator FEV1 / FVC ratio < 0.7 establishes the diagnosis of COPD. Asthma and COPD commonly coexist butCompared to the baseline FEV1 value, asthmatic patients will have 12% or greater improvement after 15 minutes use of short-acting beta2 agonist inhalation and the FEV1 also increases by> 200 ml.

CHEST X-RAY:

Emphysematous changes-Hypertransluency, Transluency extends anteriorly up tothe 7^{th} rib and posteriorly up to 9^{th} rib. The other features are a Widened intercostal space along with low flat diaphram, tubular heart, increased pulmonary vascular markings and pulmonary artery dilatation.

FULL BLOOD COUNT AND HAEMATOCRIT:

To identify anemia, polycythemia andleukocytosis

SPUTUM CULTURE:

For identification of theorganism.

BODY MASS INDEX (BMI):

For theassessment of prognosis.

ALPHA-1 ANTITRYPSIN:

Alpha-1 antitrypsin deficiency is an uncommon, but not rare a condition associated with premature emphysema. Testing for α1-antitrypsin deficiency is indicated in the likely hood of having the disorder.

Conditions suggesting alpha-1 anti-trypsin deficiency
Early-onset emphysema (age under 45 years)
Emphysema in a nonsmoker
Emphysema predominantly in lung bases (pan-acinar)
Necrotizing panniculitis (Weber-Christian disease)
c-ANCA positive vasculitis (e.g., Wegener's granulomatosis)
Family history of early onset emphysema or non-smoking–related emphysema
Bronchiectasis without other etiology

A serum alpha-1 antitrypsin concentration level below 15-20% of the normal value is highly suggestive of homozygous alpha-1 antitrypsin deficiency.

Transfer factor for carbon monoxide (TLCO) and transfer coefficient (KCO):

To investigate symptoms thatseems disproportionate to the Spiro metric impairment. The transfer factor test for carbon monoxide measures the ability to move carbon monoxide from inhaled gas to hemoglobin in the alveolar capillaries. A reduction in transfer factor (TLCO) and transfer coefficient (KCO) is the best functional indicator of the presence and severity of pulmonary emphysema.[107]

In this context KCO is more specific than TLCO.[108] Asthma may reduce TLCO when severe but KCOtends to be high in asthma. Emphysema with its destruction of alveolar capillary membrane results in large air space, decreased area for gas transfer & reduction of TLCO & KCO.

PULSE OXIMETRY:

Assessthe Spo_2level and need for oxygen therapy.

If corpulmonale present, or if FEV1 < 50% predicted it is indicated.

ARTERIAL BLOOD GAS MEASUREMENT:

In acute exacerbations of COPD,to confirm the degree of hypoxemia and hypercapnia the arterial blood gases measurement is important.It is recommendedin FEV1 <40%, signs of respiratory failure or right heart failure. In acute exacerbationblood gas analysis evaluates the severity, prognosis, the need for oxygen therapy with reference to invasive or noninvasive ventilator support.

CT SCAN OF THE THORAX:

CT chest is recommended only if there is a doubt inthe diagnosis of COPD.

ECG:

The characteristic ECG pattern in patients with chronic obstructive pulmonary disease is due to the insulating effect of the hyperinflated lungs,altered position of the of the heart, and caudal displacement of the diaphragm.

ECG changes in COPD

1. P waves >0.25 mV in lead II, III, or aVF – P pulmonale.
2. P wave axis to the right of 80 degrees in the frontal plane.
3. Lead I sign with an isoelectric P wave, QRS amplitude <0.15 mV, and T wave amplitude<0.05 mV
4. QRS amplitude in all limb leads <0.5 mV
5. QRS axis to the right of 90 degrees in the frontal plane
6. QRS amplitude <0.5 mV in lead V5 or V6; or R wave <0.7 mV in lead V5 or R wave <0.5 mV in lead V6
7. R/s >1 in V1 or R wave amplitude in V1 >5 mm, R/S ratio <1 in lead V5 or V6
8. S1S2S3 pattern with R/S ratio <1 in leads I, II, and III- $S_1S_2S_3$ syndrome.
9. Complete/ incomplete right bundle branch block

10.T wave - decrease in amplitude in all leads, may be inverted in right precordial leads

11. Right ventricle hypertrophy:

- Prominent terminal S waves in the left precordial leads.

- Right axis deviation.

ECHOCARDIOGRAPHY:

Echocardiography is sensitive test to detect pulmonary hypertension, corpulmonale and left ventricular dysfunction in COPD patients. It is aneasily available, non-invasive technique that assesses the right ventricular hypertrophy, dilatation,pulmonaryartery pressure and ejection flow dynamics. In COPD patients,the hyperinflated lungs alter the sound wave transmission.[109] Two-dimensional echocardiography gives important information on dynamics of cardiac structures and morphology [110].Continuous wave Doppler echocardiography may provide an estimate of pulmonary artery systolic pressure in the presence of tricuspid regurgitation.

Echocardiography findings in COPD:

Increase the pulmonary artery pressure.

Tricuspid regurgitation.

Right ventricular wall thickening.

Increaseright ventricular volume.

Reverse movement of the inter-ventricular septum.

Right atrium and ventricle enlargement

Left ventricular cavity may be normal or reduced

Right ventricular dysfunction.

Systolic bowing of the inter-ventricular septum towards the left ventricle is a characteristic abnormality of right ventricular pressure overload and it is detected by two-dimensional echocardiography.[111]In patients who are difficult to image with 2-D echocardiography, MRI is usefulfor assessing RV structure. Pulmonary hypertensiondiagnosis is confirmed by Right-heart catheterization

BNP AND N-TERMINAL BNP:

In corpulmonale BNP and N-terminal BNP levels are elevated,secondary to RV stretch. The severity of pulmonary hypertension and right ventricular distension may be estimated by BNP levels and also reflects the treatment efficacy.

MANAGEMENT:

The overall approach to managing stable COPD should be characterized by an increase in treatment,depending on the severity of the disease and the clinical status of the patients.

The therapeutic goals are:

1. Preventprogression ofdisease (cessation of smoking)
2. Relive thedyspnea and respiratory symptoms

3.Improve daily activity and exercise tolerance

4. Decrease the frequency and severity of exacerbations

5. Treat the COPD exacerbations and complications.

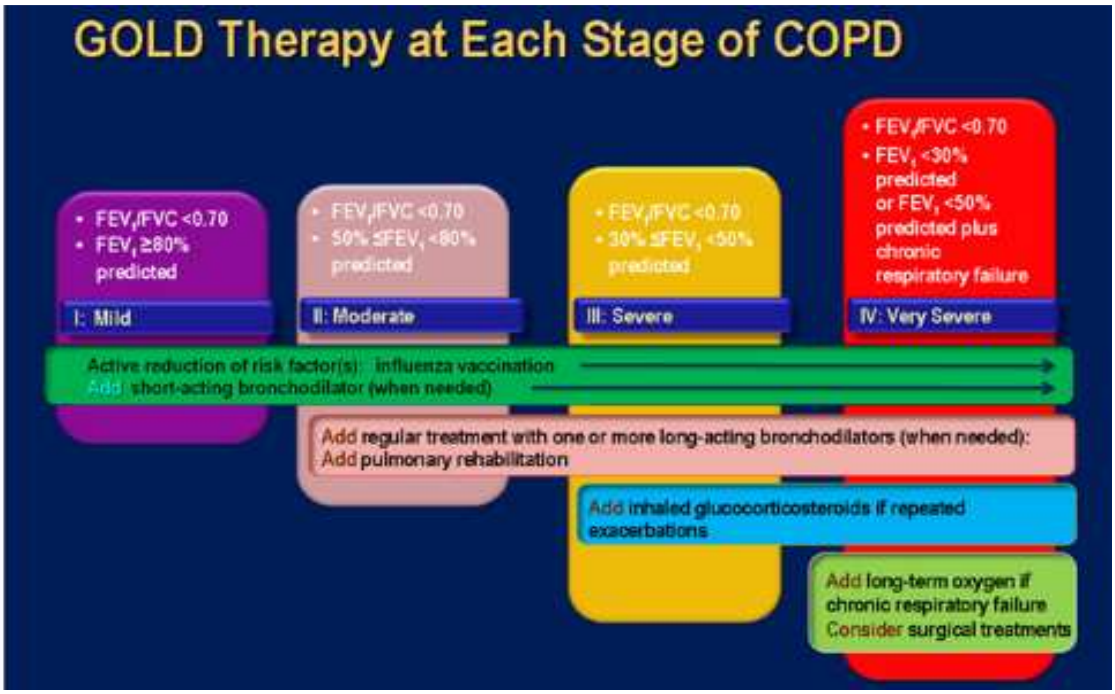
6.Improve the health status

7. Mortality reduction

Management strategies arepharmacotherapy and non-pharmacotherapeutic approaches that improve quality of life, activity levels and symptoms of COPD.

PHARMACOTHERAPY:

Pharmacological treatment of COPD has to improve the symptoms, reduceexacerbations, hospitalizations, and improve the quality of life.Inhaled bronchodilators, corticosteroids, oral theophylline and oral phosphodiesterase-4 inhibitor are useful in COPD.



Bronchodilators are the mainstay in COPD pharmacotherapy. Bronchodilators reduce air trapping, breathlessness and improve quality of life. Bronchodilators can increase FEV1<10%.[52]Patients with mild COPD should be started onshort-acting inhaled beta2 agonist or ipratropium. If symptoms persist ipratropium(tiotropium) or long-acting beta2 agonist (LABA)) is an alternative. Concurrent use of tiotropium and ipratropium is not routinely recommended.

In moderate to severe COPD, the treatment iscombination of tiotropium and LABA.In recurrent exacerbations add inhaled steroids.[112]In acute exacerbations of COPD inhaled and systemic steroids have more beneficial.[113,114]. Inhaled steroids have been shown to improve the lung function, symptoms,quality of life and to reduce the frequency of COPD exacerbations.[115,116,117] Long-term inhaled

corticosteroids use associated with an increased risk of pneumonia.[52] Oral corticosteroids have numerous side effects so it is not recommended as a long-term monotherapy.[52]

Theophylline is useful in persistent symptoms despite optimal inhaled therapy. Roflumilast is a phosphodiesterase-4 (PDE-4)inhibitor, it inhibit the intracellular cyclic AMP breakdown and reduces the inflammation. It is administered 500 mg OD orally and it reduces acute exacerbations.[118]Roflumilast used concurrently with LABA has been shown to reduce the acute exacerbations.[119,120]

OXYGEN THERAPY:

The main goal of oxygen therapy is to maintain SpO2 ≥ 90% or PaO2 ≥ 60 mmHg atrest. Supplemental O_2 is routinely used for patients with exertional or nocturnal hypoxemia.Long-term oxygen therapy (LTOT) (>15 h per day) is useful in respiratory failure and with severe resting hypoxemia and has been found to have increased survival.[52]

IMMUNIZATION OF THE PNEUMOCOCCAL AND INFLUENZA INFECTIONS:

Pneumococcal vaccination for every 5-10 years

Influenza vaccination for yearly

NON-PHARMACOLOGIC TREATMENT:

SMOKING CESSATION

In long-term smokerscessation ofsmoking is more effective to prevent the progress of the disease and has been found to reduce the decline of FEV1.

PULMONARY REHABILITATION:

The components of pulmonary rehabilitation programme includesmoking cessation,nutrition counselling, exercise training and education.

SURGICAL TREATMENT:

Lung volume reduction surgery is indicated in upper lobe emphysema.

Lung transplantation**:**

Lung transplantation is indicated in COPD patients who have FEV1 < 25% predicted or the paCO2 is > or = 55 mm Hg.

In respiratory failure either non-invasive mechanical ventilation or mechanical ventilation indicated.

CORPULMONALE:

The primary treatment of corpulmonale consists of continuous oxygen to overcome hypoxemia and diuretics to control peripheral edema. Digitalis is useful for rate control of atrial fibrillation.

PROGNOSIS:

Factors that predict poor survival in COPD are low FEV1, active smoking

status, hypoxemia, poor nutrition, the presence of corpulmonale, resting tachycardia, low exercise capacity, severe dyspnea, poor health-related quality of life, anemia, frequent exacerbations, co-morbid illnesses, and low carbon monoxide diffusing capacity. COPD prognosis is based onthe BODE index.

Calculation of the BODE Index*

	Points on the BODE Index			
Variable	**0**	**1**	**2**	**3**
FEV_1 (% predicted)	≥65	50–64	36–49	≤35
Distance walked in 6 min (meters)	≥350	250–349	150–249	≤149
MMRC dyspnea scale	0–1	2	3	4
Body-mass index (kg/M^2)	> 21	≥21		

BODE score greater than 7 is associated with a 30 percent 2-year mortality.

Score of 5 to 6 is associated with 15 percent 2-year mortality.

Score is less than 5, the 2-year mortality is less than 10 percent.

AIM OF THE STUDY:

To study the prevalence of LV systolic dysfunction in COPD patients and to assess the possible risk factors contributing to the development of LV systolic dysfunction.

METHODS AND MATERIALS:

Study group : COPD patients admitted in the department of General Medicine

Study design : Observational study

Place of Study : Govt. Royapettah Hospital

Sample size : 50 patients

Duration of study : 6 months (May 2013-October 2013)

Conflict of interest: Nil

Hazards to study population: Nil

Clearance was obtained from the ethical committee of Government Kilpauk Medical College.

METHODOLOGY:

In patients with COPD, CBC with ESR, RBS, FBS, PPBS, Blood urea & creatinine, lipid profile, LFT, Urine Routine, Ultra sonogram Abdomen, Chest X-ray, Pulse Oximetry for SPO2, Pulmonary function test, ECG, ECHO will be done after obtaining written informed consent. Severity COPD is assessed by Gold criteria. LVEF was measured by 2D Echo. PFT was assessed by Spirometry. LVEF was compared with severity of COPD and possible risk factor behind such development.

Inclusion criteria :

AllCOPD patients.

Exclusion criteria :

1. Systemic Hypertension
2. Diabetes Mellitus
3. H/o congenital, acquired valvular heart disease
4. IHD
5. Cardiac arrythmias

6. Chronic AF
7. Complete RBBB or LBBB
8. H/o heart failure
9. Chronic kidney disease
10. Patients with poor echo window
11. Patients unable to perform PFT

Data collection:

The data of each patient will be collected in a specifically prepared proforma and includes demographic details proper history, clinical features, CBC with ESR, RFT, FBS, PPBS, LFT, Total Cholesterol& Triglycerides, Ultrasound Abdomen, chest X-ray, ECG, PFT and ECHO

A diagnosis of COPD should be considered in:

Persistent cough with expectoration for 3 months in two consecutive years

Chronic cough - Present intermittently or present throughout the day

Chronic sputum production

Dyspnea that is- Progressive (worsens over time)

- Persistent (present everyday)
- Worse on exercise
- Worsens during respiratory infections

Leg swelling for corpulmonale

History of exposure to risk factors –smoking, air pollution

On examination: pallor, edema, elevated JVP,purse lip breathing,pulse,CVS-P_2loud,RS-wheeze,crepitations.

Chest X-ray: evidence of Hypertransluency, low flat diaphragm,widened intercostal space, and tubular heart.

SPIROMETERY:

COPD is diagnosed only if FEV1 <80%predicted and FEV1/FVC <0.7

(mild COPD FEV1 >80% predicted)

Performance of Spirometery:

Spirometry was done according to the guidelines published by the British Thoracic Society. Patient's sex, age and height are entered in the spirometer.Patientswereseated comfortablyandmaneuver demonstrated. They were asked to take deep full inspiration. Good seal was maintained with the mouth piece of spirometry.Patients were asked to blow the breath out, forcibly as hard and as fast as possible, until there is nothing left to expelfor at least 6 seconds and to a maximum of 15seconds.The results (FEV_1 & FEV_1/FVC) appear on the display andare noted. The results of the measurement were accepted only smooth & cough free. This maneuver was repeated three times. Best of the three consistent readings of FEV1 and FVC were taken.Reversibility test was done thirty minutes after200

mcgof salbutamolnebulization to rule out bronchial asthma (reversibility more than 12% FEV_1&FEV1 increases> 200 ml).

Calculation of % improvement

FEV1 (post bronchodilator) – FEV1 (base line)

---------- X 100

FEV1 (base line)

FEV1 / FVC % < 70 is used to diagnose COPD

For assessment of Severity of COPD by FEV1%

The COPD severity was assessed by GOLD criteria.

GOLD Stage	Severity	Symptoms	Spirometry
0	At Risk	Chronic cough, sputum production	Normal
I	Mild	With or without chronic cough or sputum production	FEV_1/FVC <0.7 and FEV_1 ≥80% predicted
IIA	Moderate	With or without chronic cough or sputum production	FEV_1/FVC <0.7 and 50% ≤FEV_1 <80% predicted
III	Severe	With or without chronic cough or sputum production	FEV_1/FVC <0.7 and 30% ≤FEV_1 <50% predicted
IV	Very Severe	With or without chronic cough or sputum production	FEV_1/FVC <0.7 and FEV_1 <30% predicted or FEV_1 <50% predicted with respiratory failure or signs of right heart failure

Electrocardiograph was taken and looked for evidence of pulmonary hypertension in chronic obstructive airways disease.

All patients were subjected to both 2 D and Doppler Echocardiogram

THE FOLLOWING PARAMETERS ARE OBTAINED FROM ECHOCARDIOGRAM.

EJECTION FRACTION**:**

M-mode or two-dimensional echocardiographic measurement of LV dimensionfrom the mid-ventricular level is used to calculate LVEF as follows:

$LVEF = (LVEDD^2 – LVESD^2) / LVEDD^2$

EF-50% - 75%is normal.**EF <50% istaken as LV systolic dysfunction.**

DIASTOLIC FUNCTION OF THE LV:

The trans mitral pressure gradient or the relationship between LA and LV Pressures are accurately reflected by mitral inflow Doppler velocities. Diastolic filling is usually classified initially on the basis of the peak mitral flow velocity of the early rapid filling wave (E), peak velocity of the late filling wave caused by atrial contraction (A), E/A ratio, and deceleration time (DT), which is the time interval for the peak E velocity to reach zero baseline. Diastolic dysfunction can be graded according to the diastolic filling pattern.

Grade 1 -mild dysfunction-(E/A ratio <1.0 and DT >240 milliseconds).

Grade 2 -moderate dysfunction- (E/A ratio of 1 to 1.5 and normal DT 160 to 240 milliseconds).

Grade 3 (severe reversible dysfunction)&Grade 4 (severe irreversible dysfunction) –(E/A ratio higher than 2, and shortened DT < 160 milliseconds)

PULMONARY ARTERY PRESSURES:

Flow velocities recorded with Doppler echocardiography are used to determine various intra-cardiac pressures. Pulmonary artery systolic pressure equal to the calculated RV systolic pressure. RV systolic pressure can be obtained by adding the estimated RA pressure to the TR velocity.TR velocity reflects the systolic pressure difference between the right ventricle and rightatrium .Tricuspid regurgitation velocity was recording by continuous-wave Doppler echocardiography.

PA pressure levelsin PHT.

PHT GRADE	PA PRESSURE
MILD	30 – 50 mmHg
MODERATE	50 – 80 mmHg
SEVERE	>80 mmHg

PULMONARY VELOCITY ACCELERATION TIME(PVAT):

There may be situations in which no tricuspid regurgitation is present or the signal is inadequate to obtain reliable measurements. PVAT also used toassess the severity of PHT.

PHT SEVERITY	PVAT
Normal	>120 milliseconds
MILD	100 – 120 milliseconds
MODERATE	80 – 100 milliseconds
SEVERE	<80 milliseconds

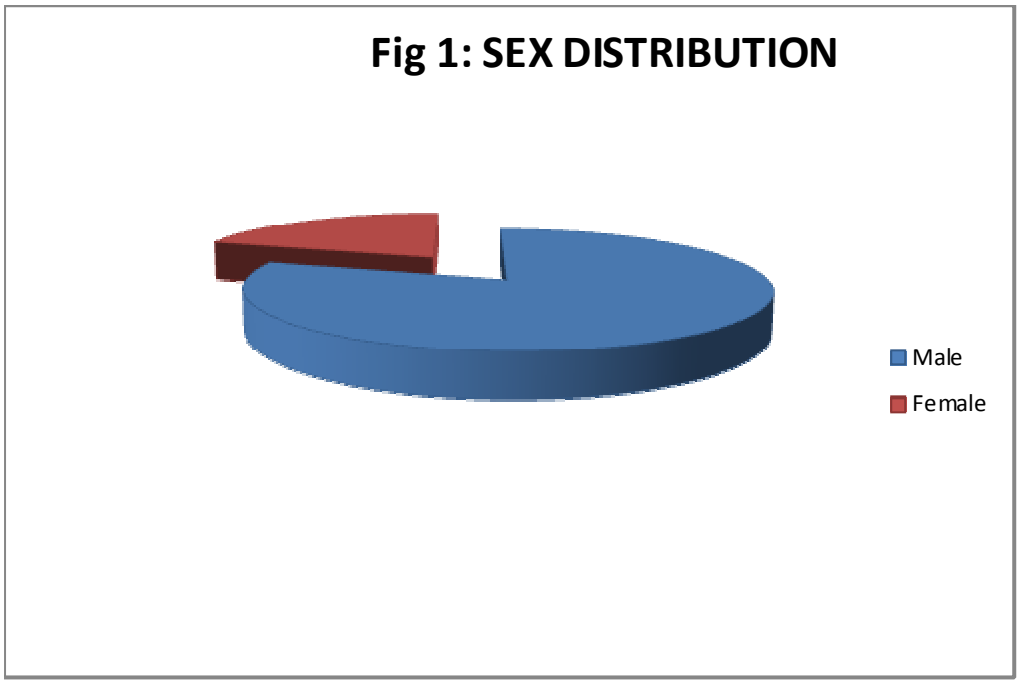
RA/RV dilation and main pulmonary artery diameter noted and correlated with the severity of PHT.

OBSERVATION

Table1: SEX DISTRIBUTION:

Sex group	Frequency	Percentage
Male	40	80.0
Female	10	20.0

Age (years)	Frequency	Percentage
Total	50	100.0



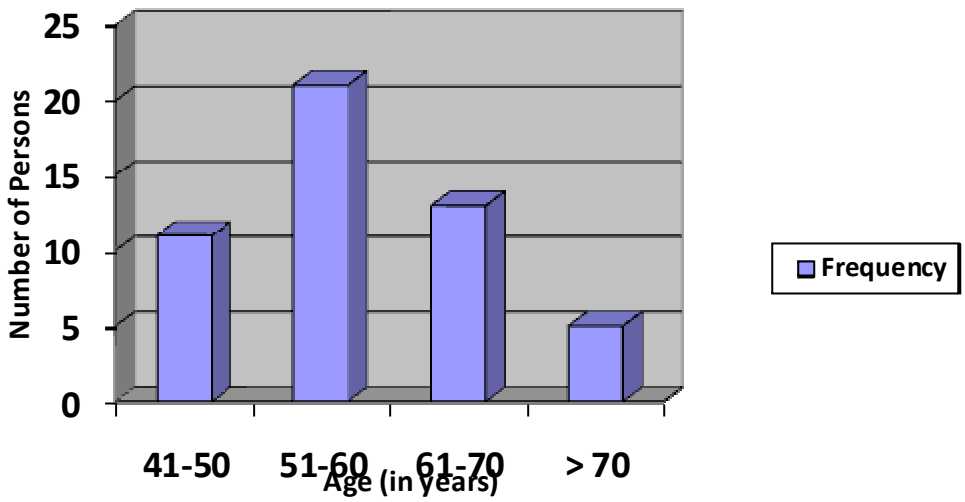
In our study the prevalence of COPD is more in males. Male: Female ratio is 4:1.

Table 2: AGE DISTRIBUTION:

41-50	11	22.0
51-60	21	42.0
61-70	13	26.0
> 70	5	10.0
Total	50	100.0

Lower age limit 40 was selected because many of the studies reported thatthe

Fig 2: AGE DISTRIBUTION

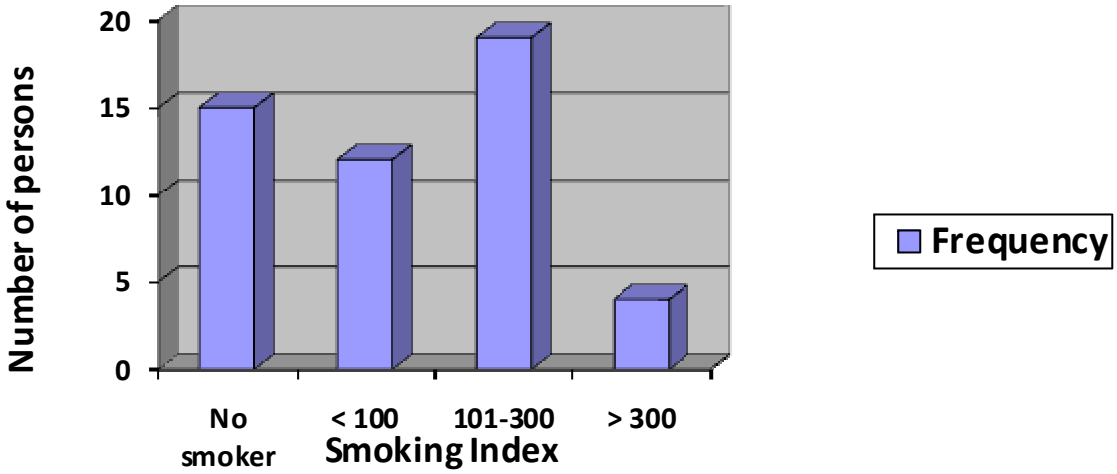


overall prevalence of COPD is higher in age group more than 40 years. In ourstudy prevalence of COPD is more in the age group 51 – 60 years. i.e., 42% of patients belong to 51- 60 years.

Table 3:SMOKING INDEX AND COPD

Smoking Index	Frequency	Percentage
No smoker	15	30.0
< 100	12	24.0
101-300	19	38.0
> 300	4	8.0
Total	50	100.0

Fig 3: Smoking Index and COPD



Smoking index is taken as a parameter because in India number of cigarettes,

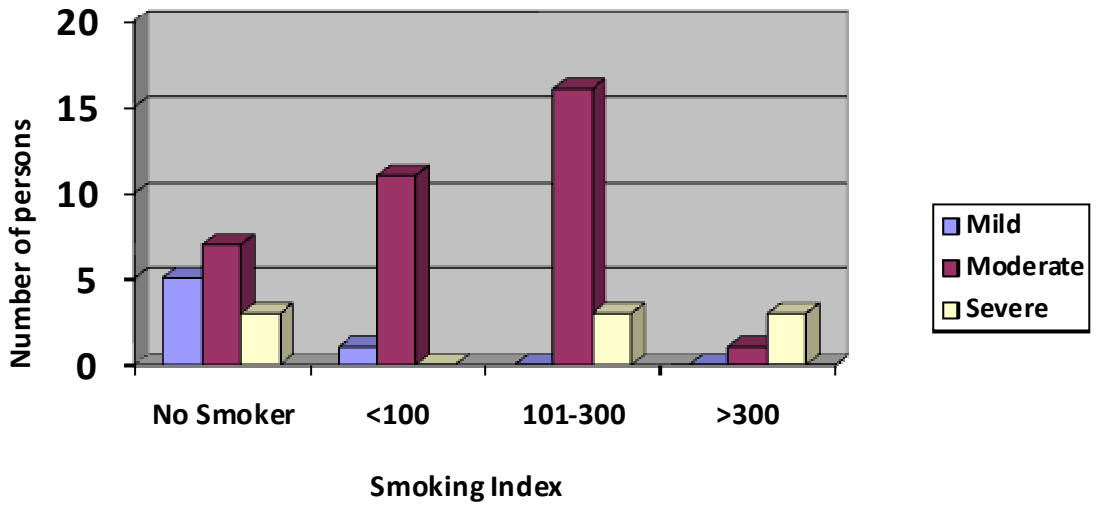
Beedis per pocket were quiet variable and weight of Beedis is widely different in different brands. More importantly Indian smokers often describe their smoking habit by the total number of cigarettes/Beedis per day rather than the number of pockets[121].

SMOKING INDEX	GRADE
<100	Mild smoker
101 – 300	Moderate smoker
>300	Heavy smoker

38% of our subjects were moderate smokers and 30% were nonsmokers

.

Fig 4 :Smoking Index and Severity of COPD



Majority of the smokers have moderate to severe COPD. 91.7% mild smokers and

84.2% of the moderate smokers had moderate COPD. 75% heavy smokers have severe COPD.“p” value is significant. Severity of COPD is directlyrelated to the smoking index .

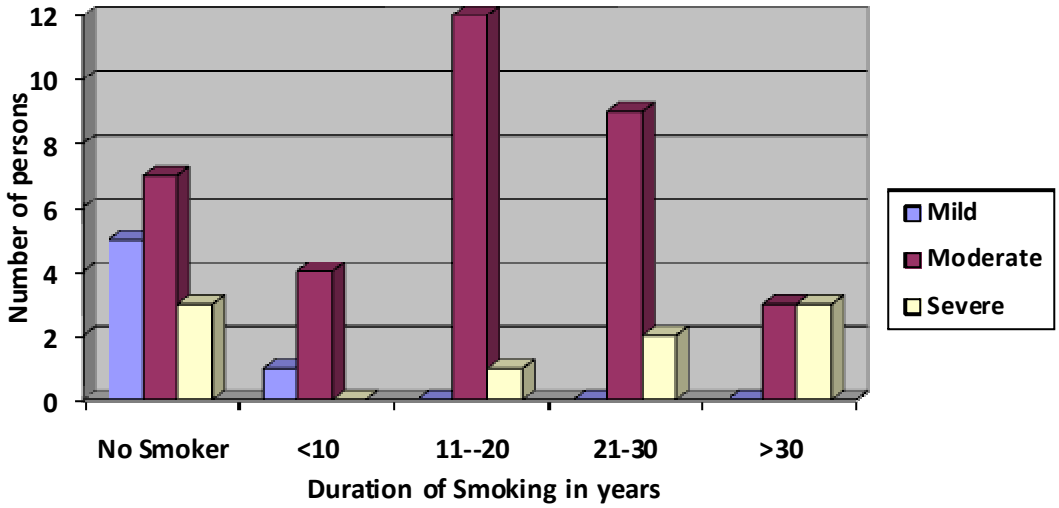
Table 4:SMOKING INDEX AND SEVERITY OF COPD

Smoking Index		Severity of COPD			Total	p value
		Mild	Moderate	Severe		
Non smoker	Number of persons	5	7	3	15	0.001**
	% of nonsmokers	33.3%	46.7%	20.0%	100.0%	
	% within Severity of COPD	83.3%	20.0%	33.3%	30.0%	
< 100	Number of persons	1	11	0	12	
	% within Smoking Index	8.3%	91.7%	.0%	100.0%	
	% within Severity of COPD	16.7%	31.4%	.0%	24.0%	
101-300	Number of persons	0	16	3	19	
	% within Smoking Index	.0%	84.2%	15.8%	100.0%	
	% within Severity of COPD	.0%	45.7%	33.3%	38.0%	
> 300	Number of persons	0	1	3	4	
	% within Smoking Index	.0%	25.0%	75.0%	100.0%	
	% within Severity of COPD	.0%	2.9%	33.3%	8.0%	
Total	Number of persons	6	35	9	50	
	% within Smoking Index	12.0%	70.0%	18.0%	100.0%	
	% within Severity of COPD	100.0%	100.0%	100.0%	100.0%	

Table 5: DURATION OF SMOKING AND SEVERITY OF COPD

Duration of Smoking in years		Severity of COPD			Total	p value
		Mild	Moderate	Severe		
Non smoker	Number of Persons	5	7	3	15	
	% among nonsmokers	33.3%	46.7%	20.0%	100.0%	
	% within Severity of COPD	83.3%	20.0%	33.3%	30.0%	
< 10	Number of Persons	1	4	0	5	
	% within Duration of Smoking in years	20.0%	80.0%	.0%	100.0%	
	% within Severity of COPD	16.7%	11.4%	.0%	10.0%	
11-20	Number of Persons	0	12	1	13	
	% within Duration of Smoking in years	.0%	92.3%	7.7%	100.0%	
	% within Severity of COPD	.0%	34.3%	11.1%	26.0%	
21-30	Number of Persons	0	9	2	11	
	% within Duration of Smoking in years	.0%	81.8%	18.2%	100.0%	.026*
	% within Severity of COPD	.0%	25.7%	22.2%	22.0%	
> 30	Number of Persons	0	3	3	6	
	% within Duration of Smoking in years	.0%	50.0%	50.0%	100.0%	
	% within Severity of COPD	.0%	8.6%	33.3%	12.0%	
Total	Number of Persons	6	35	9	50	
	% within Duration of Smoking in years	12.0%	70.0%	18.0%	100.0%	
	% within Severity of COPD	100.0%	100.0%	100.0%	100.0%	

Fig 5: Duration of Smoking and Severity of COPD



In our study report those who smoked more than 10 years had moderate to severe obstruction and 50% of the smokerswho smoked more than 30 years had severe obstruction. 'p' value is significant. prolonged duration of smoking is associated with Increased severity of COPD.

Fig 6 : Socio Economic Status and Severity of COPD

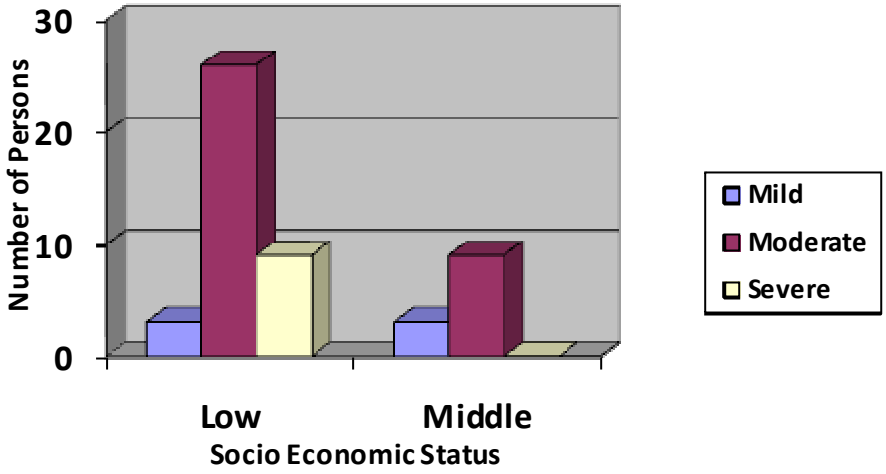


Table 6:SOCIO ECONOMIC STATUS AND SEVERITY OF COPD

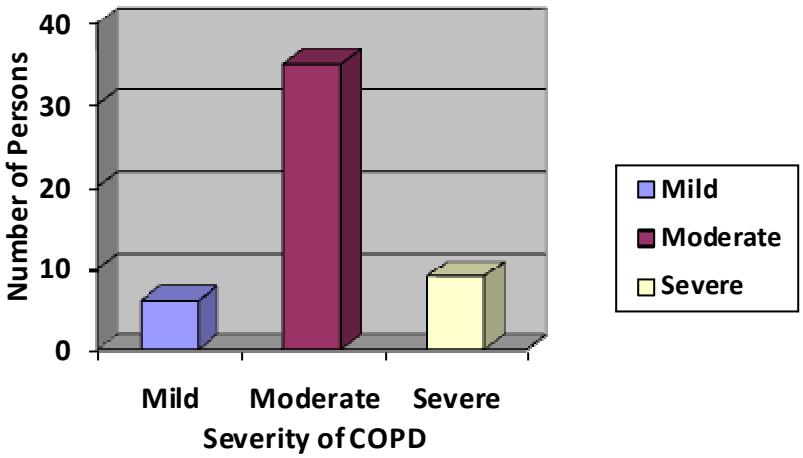
Socio Economic Status		Severity of COPD			Total	p value
		Mild	Moderate	Severe		
Low	Number of Persons	3	26	9	38	0.03*
	% within Socio Economic Status	7.9%	68.4%	23.7%	100.0%	
	% within Severity of COPD	50.0%	74.3%	100.0%	76.0%	
Middle	Number of Persons	3	9	0	12	
	% within Socio Economic Status	25.0%	75.0%	.0%	100.0%	
	% within Severity of COPD	50.0%	25.7%	.0%	24.0%	
Total	Number of Persons	6	35	9	50	
	% within Socio Economic Status	12.0%	70.0%	18.0%	100.0%	
	% within Severity of COPD	100.0%	100.0%	100.0%	100.0%	

Economic status is inversely related to COPD. Our study shows 76% of the COPD patients belong to low socio economic status due to poor housing condition, overcrowding, poor environment, poor nutrition, alcohol, smoking and recurrent lower respiratory infections.

Table 7:SEVERITY OF COPD DISTRIBUTION

Severity of COPD	Frequency	Percent
Mild	6	12.0
Moderate	35	70.0
Severe	9	18.0
Total	50	100.0

Fig 7: Severity of COPD Distribution

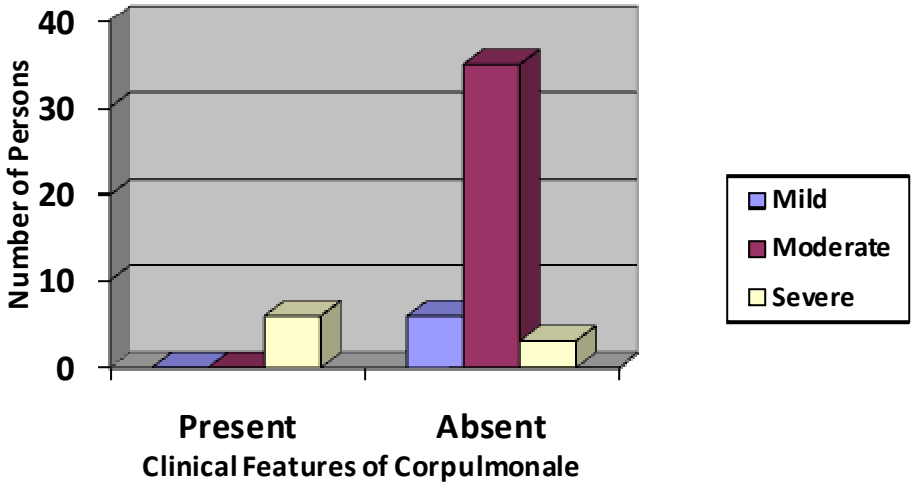


Most of them are (70%) are moderate COPD.

Table 8: CORPULMONALE AND SEVERITY OF COPD

Clinical Features of Corpulmonale		Severity of COPD			Total	p value
		Mild	Moderate	Severe		
Present	Number of Persons	0	0	6	6	<0.001**
	% within Clinical Features of Corpulmonale	.0%	.0%	100.0%	100.0%	
	% within Severity of COPD	.0%	.0%	66.7%	12.0%	
Absent	Number of Persons	6	35	3	44	
	% within Clinical Features of Corpulmonale	13.6%	79.5%	6.8%	100.0%	
	% within Severity of COPD	100.0%	100.0%	33.3%	88.0%	
Total	Number of Persons	6	35	9	50	
	% within Clinical Features of Corpulmonale	12.0%	70.0%	18.0%	100.0%	
	% within Severity of COPD	100.0%	100.0%	100.0%	100.0%	

Fig 8: Corpulmonale and Severity of COPD

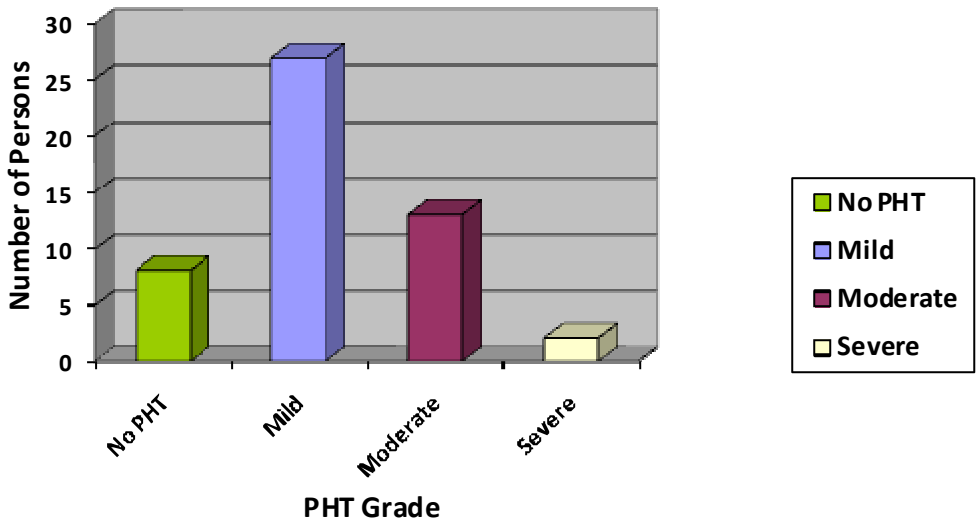


'p' value is highly significant. All patients with corpulmonale had severe obstructive pattern. 66.7% of severe COPD patients developed corpulmonale.

Table 9: PHT in COPD

PHT Grade	Frequency	Percent
No PHT	8	16.0
Mild	27	54.0
Moderate	13	26.0
Severe	2	4.0
Total	50	100.0

Fig 9: PHT in COPD



Our study reports that 84% of them have pulmonary hypertension. This is due to chronic hypoxia in COPD that may the reason for pulmonary hypertension. Out of these 54% of them have mild, 26% moderate and 4% severe PHT.

Fig 10 : Smoking Index and PHT

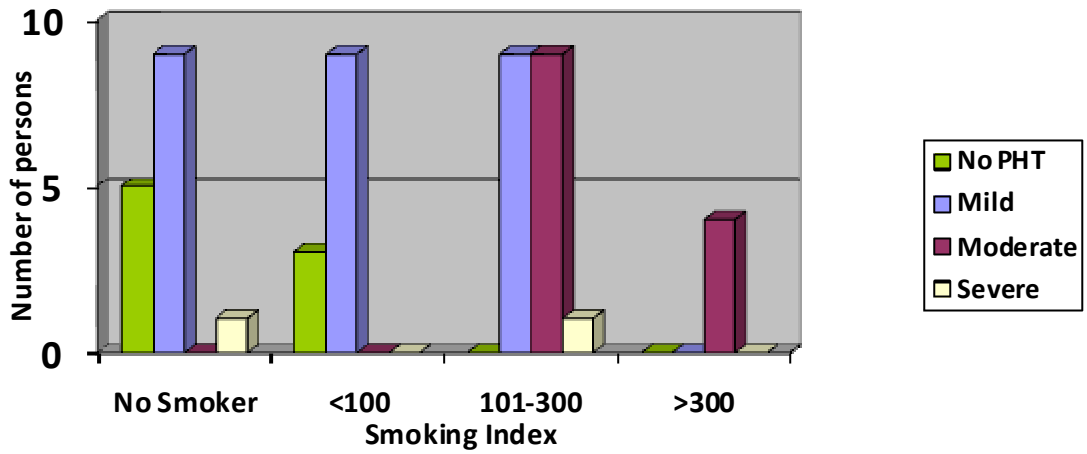


Table 10: SMOKING INDEX AND PHT

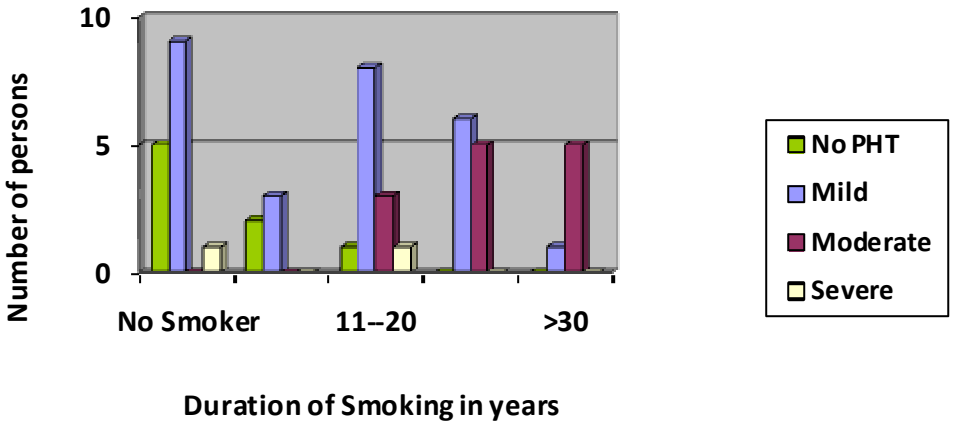
Smoking Index		PHT Grade				Total	p value
		No PHT	Mild	Moderate	Severe		
Non smoker	Number of persons	5	9	0	1	15	
	% nonsmoker	33.3%	60.0%	.0%	6.7%	100.0%	
	% within PHT Grade	62.5%	33.3%	.0%	50.0%	30.0%	
< 100	Number of persons	3	9	0	0	12	
	% within Smoking Index	25.0%	75.0%	.0%	.0%	100.0%	
	% within PHT Grade	37.5%	33.3%	.0%	.0%	24.0%	
101-300	Number of persons	0	9	9	1	19	<0.001**
	% within Smoking Index	.0%	47.4%	47.4%	5.3%	100.0%	
	% within PHT Grade	.0%	33.3%	69.2%	50.0%	38.0%	
> 300	Number of persons	0	0	4	0	4	
	% within Smoking Index	.0%	.0%	100.0%	.0%	100.0%	
	% within PHT Grade	.0%	.0%	30.8%	.0%	8.0%	
Total	Number of persons	8	27	13	2	50	
	% within Smoking Index	16.0%	54.0%	26.0%	4.0%	100.0%	
	% within PHT Grade	100.0%	100.0%	100.0%	100.0%	100.0%	

PHT severity is more in moderate and heavy smokers than mild smokers. ‘p’ value is highly significant. PHT severity found to be directly correlate with smoking index.

Table 11: DURATION OF SMOKING AND PHT

Duration of Smoking in years		PHT Grade				Total	p value
		No PHT	Mild	Moderate	Severe		
Non smoker	Number of persons	5	9	0	1	15	.012*
	%among nonsmokers	33.3%	60.0%	.0%	6.7%	100.0%	
	% within PHT Grade	62.5%	33.3%	.0%	50.0%	30.0%	
< 10	Number of persons	2	3	0	0	5	
	% within Duration of Smoking in years	40.0%	60.0%	.0%	.0%	100.0%	
	% within PHT Grade	25.0%	11.1%	.0%	.0%	10.0%	
11-20	Number of persons	1	8	3	1	13	
	% within Duration of Smoking in years	7.7%	61.5%	23.1%	7.7%	100.0%	
	% within PHT Grade	12.5%	29.6%	23.1%	50.0%	26.0%	
21-30	Number of persons	0	6	5	0	11	
	% within Duration of Smoking in years	.0%	54.5%	45.5%	.0%	100.0%	
	% within PHT Grade	.0%	22.2%	38.5%	.0%	22.0%	
> 30	Number of persons	0	1	5	0	6	
	% within Duration of Smoking in years	.0%	16.7%	83.3%	.0%	100.0%	
	% within PHT Grade	.0%	3.7%	38.5%	.0%	12.0%	
Total	Number of persons	8	27	13	2	50	
	% within Duration of Smoking in years	16.0%	54.0%	26.0%	4.0%	100.0%	
	% within PHT Grade	100.0%	100.0%	100.0%	100.0%	100.0%	

Fig 11: Duration of Smoking and PHT



'p' value is significant. Duration of smoking is directly proportional to the PHT severity. Moderate PHT is present in those who are smoked more than 10 years. The percentage of moderate PHT is more in those who smoked more than 20 years.

Fig 12: Severity of COPD and Pulmonary Hypertension

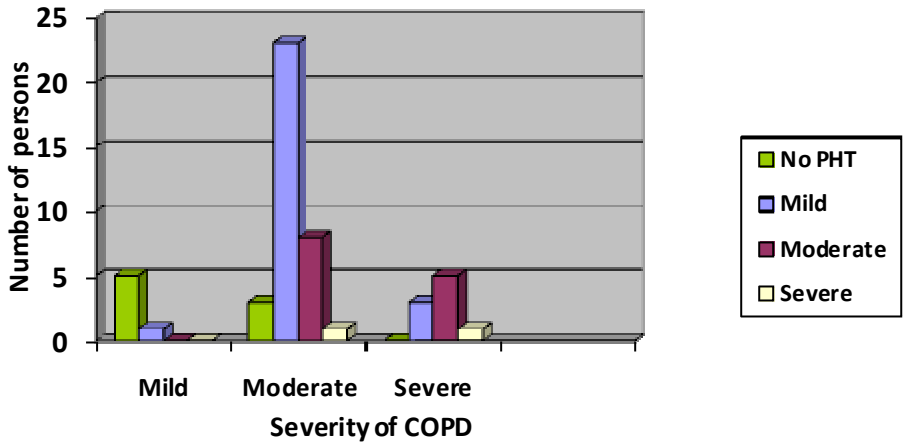


Table 12: SEVERITY OF COPD AND PHT GRADE

Severity of COPD		PHT Grade				Total	p value
		No PHT	Mild	Moderate	Severe		
Mild	Number of persons	5	1	0	0	6	
	% within Severity of COPD	83.3%	16.7%	.0%	.0%	100.0%	
	% within PHT Grade	62.5%	3.7%	.0%	.0%	12.0%	
Moderate	Number of persons	3	23	8	1	35	
	% within Severity of COPD	8.6%	65.7%	22.9%	2.9%	100.0%	
	% within PHT Grade	37.5%	85.2%	61.5%	50.0%	70.0%	
Severe	Number of persons	0	3	5	1	9	<.001**
	% within Severity of COPD	.0%	33.3%	55.6%	11.1%	100.0%	
	% within PHT Grade	.0%	11.1%	38.5%	50.0%	18.0%	
Total	Number of persons	8	27	13	2	50	
	% within Severity of COPD	16.0%	54.0%	26.0%	4.0%	100.0%	
	% within PHT Grade	100.0%	100.0%	100.0%	100.0%	100.0%	

'p' value is significant. Severity of COPD is directly related to severity of PHT.

Severe PHT is associated with moderate and severe COPD patients.

Table 13: SEVERITY OF COPD AND PHT GRADE IN CORPULMONALE

Severity of COPD		PHT Grade				Total	p value
		No PHT	Mild	Moderate	Severe		
Severe	Number of persons		1	4	1	6	0.002**
	% within Severity of COPD		16.7%	66.7%	16.7%	100.0%	
	% within PHT Grade		100.0%	100.0%	100.0%	100.0%	
Total	Number of persons		1	4	1	6	
	% within Severity of COPD		16.7%	66.7%	16.7%	100.0%	
	% within PHT Grade		100.0%	100.0%	100.0%	100.0%	

All patients with corpulmonale have a severe obstructive pattern and 66.7% have moderate PHT. 'p'value is significant.

Fig 13: Severity of COPD and PHT in Corpulmonale

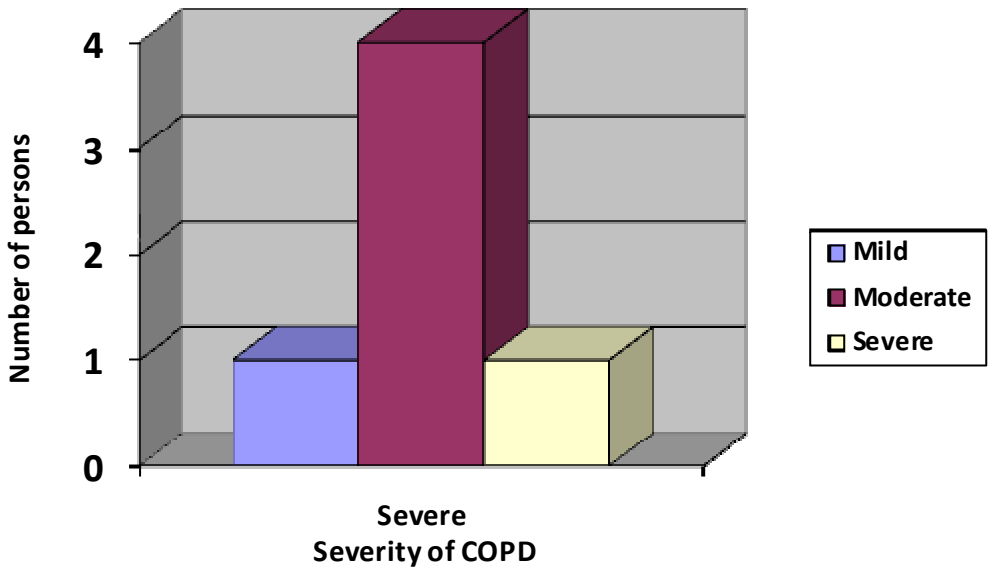
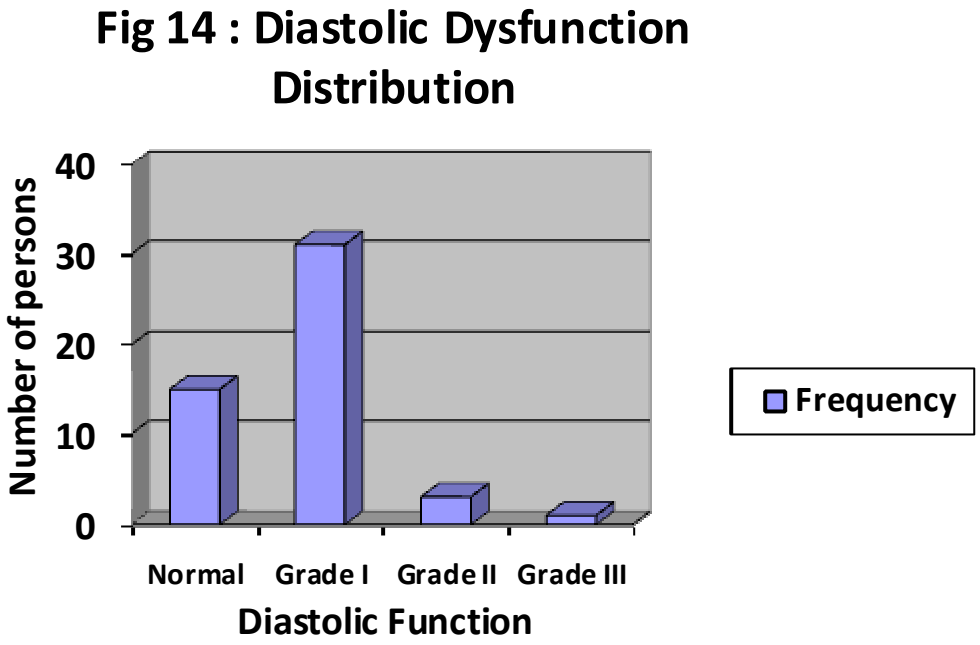


Table1:14 DIASTOLIC DYSFUNCTION DISTRIBUTIONS

Diastolic Function	Frequency	Percentage
Normal	15	30.0
Grade I	31	62.0
Grade II	3	6.0
Grade III	1	2.0
Total	50	100.0



70% of COPD patients have diastolic dysfunction in our study.

Table 15: SEVERITY OF COPD AND DIASTOLIC FUNCTION

Severity of COPD		Diastolic Function				Total	p value
		Normal	Grade I	Grade II	Grade III		
Mild	Number of persons	6	0	0	0	6	
	% within Severity of COPD	100.0%	.0%	.0%	.0%	100.0%	
	% within Diastolic Dys Function	40.0%	.0%	.0%	.0%	12.0%	
Moderate	Number of persons	9	25	0	1	35	
	% within Severity of COPD	25.7%	71.4%	.0%	2.9%	100.0%	<0.001**
	% within Diastolic Dys Function	60.0%	80.6%	.0%	100.0%	70.0%	
Severe	Number of persons	0	6	3	0	9	
	% within Severity of COPD	.0%	66.7%	33.3%	.0%	100.0%	
	% within Diastolic Dys Function	.0%	19.4%	100.0%	.0%	18.0%	
Total	Count	15	31	3	1	50	
	% within Severity of COPD	30.0%	62.0%	6.0%	2.0%	100.0%	
	% within Diastolic Dys Function	100.0%	100.0%	100.0%	100.0%	100.0%	

'p' value is highly significant. In grade1 diastolic dysfunction patients 71.4% have moderate obstruction and 19.4% have severe obstruction. In grade 2 diastolic dysfunction patients 100% have severe obstruction.COPD severity worsens the LV diastolic function. All mild COPD patients have normal LV diastolic function.

Fig 15: Severity of COPD and Diastolic Function

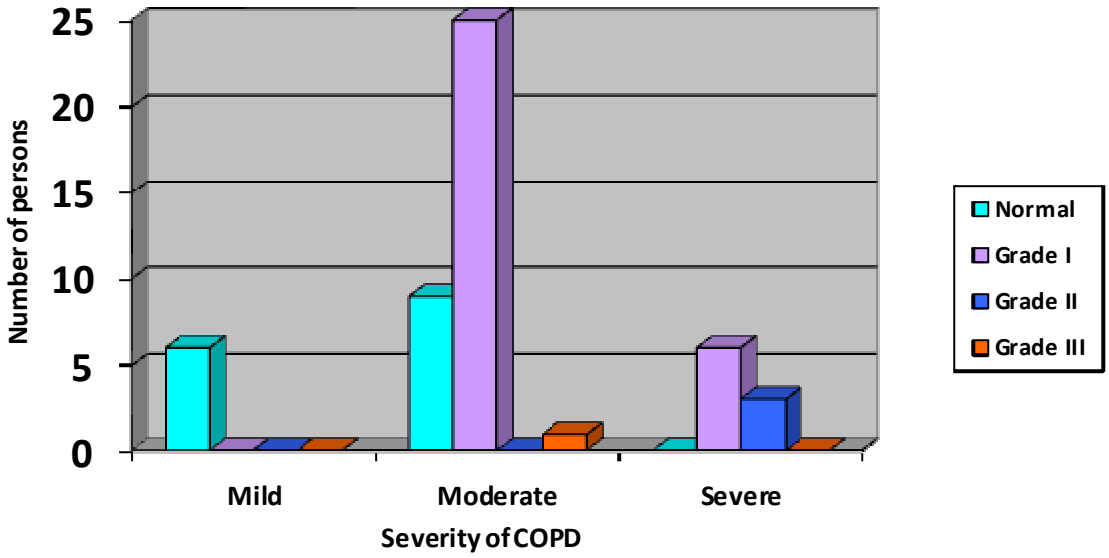


Fig 16: Pulmonary Hypertension and Diastolic Function

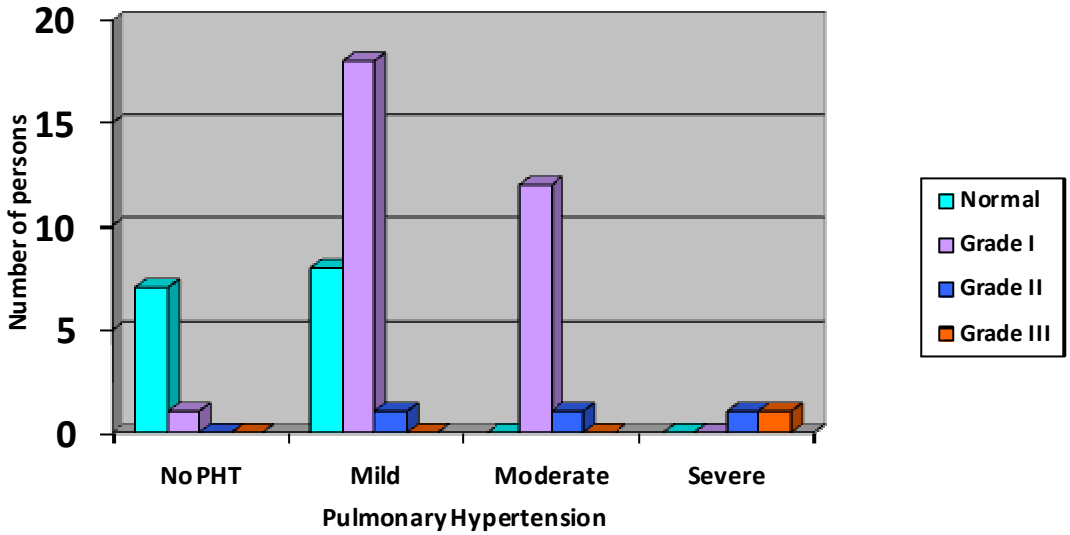


Table 16: PHT AND DIASTOLIC FUNCTION

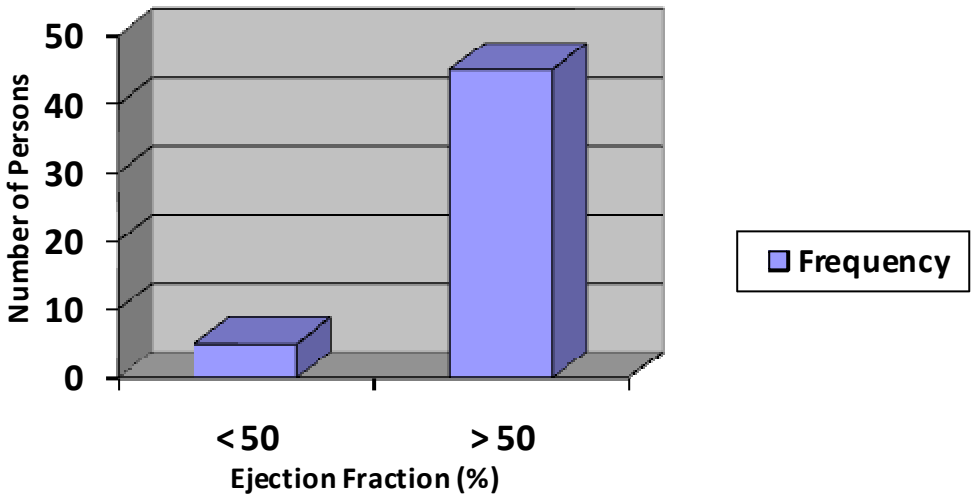
PHT Grade		Diastolic Function				Total	p value
		Normal	Grade I	Grade II	Grade III		
No PHT	Number of persons	7	1	0	0	8	<0.001**
	% No PHT	87.5%	12.5%	.0%	.0%	100.0%	
	% within Diastolic Dys Function	46.7%	3.2%	.0%	.0%	16.0%	
Mild	Number of persons	8	18	1	0	27	
	% within PHT Grade	29.6%	66.7%	3.7%	.0%	100.0%	
	% within Diastolic Dys Function	53.3%	58.1%	33.3%	.0%	54.0%	
Moderate	Number of persons	0	12	1	0	13	
	% within PHT Grade	.0%	92.3%	7.7%	.0%	100.0%	
	% within Diastolic Dys Function	.0%	38.7%	33.3%	.0%	26.0%	
Severe	Number of persons	0	0	1	1	2	
	% within PHT Grade	.0%	.0%	50.0%	50.0%	100.0%	
	% within Diastolic Dys Function	.0%	.0%	33.3%	100.0%	4.0%	
Total	Number of persons	15	31	3	1	50	
	% within PHT Grade	30.0%	62.0%	6.0%	2.0%	100.0%	
	% within Diastolic Dys Function	100.0%	100.0%	100.0%	100.0%	100.0%	

'p' value is highly significant. All severe PHT patients have grade 2-3 diastolic dysfunction.

Table 17: PREVALENCE OF LV SYSTOLIC DYSFUNCTION

Ejection Fraction (%)	Frequency	Percentage
< 50	5	10.0
> 50	45	90.0
Total	50	100.0

Fig 17:Prevalence of LV Systolic Dysfunction



Our study reports that 10% of the COPD patients have LV systolic dysfunction (EF< 50%). Out of 50 cases 5 cases have EF <50%.

Table 18: SMOKING INDEX AND LV SYSTOLIC FUNCTION

Smoking Index		Ejection Fraction		Total	p value
		< 50	> 50		
Non smoker	Number of persons	0	15	15	<0.001**
	%Non- smoker	.0%	100.0%	100.0%	
	% within Ejection Fraction	.0%	33.3%	30.0%	
< 100	Number of persons	0	12	12	
	% within Smoking Index	.0%	100.0%	100.0%	
	% within Ejection Fraction	.0%	26.7%	24.0%	
101-300	Number of persons	2	17	19	
	% within Smoking Index	10.5%	89.5%	100.0%	
	% within Ejection Fraction	40.0%	37.8%	38.0%	
> 300	Number of persons	3	1	4	
	% within Smoking Index	75.0%	25.0%	100.0%	
	% within Ejection Fraction	60.0%	2.2%	8.0%	
Total	Number of persons	5	45	50	
	% within Smoking Index	10.0%	90.0%	100.0%	
	% within Ejection Fraction	100.0%	100.0%	100.0%	

'p' value is highly significant. Moderate and heavy smokers have LVsystolic dysfunction. In moderate smokers 10.5% have LVEF<50%. But in heavy smokers 75% have LVEF<50%.Smoking index is inversely related to the LV

systolicfunction.

Fig 18: Smoking Index and LV Systolic Function

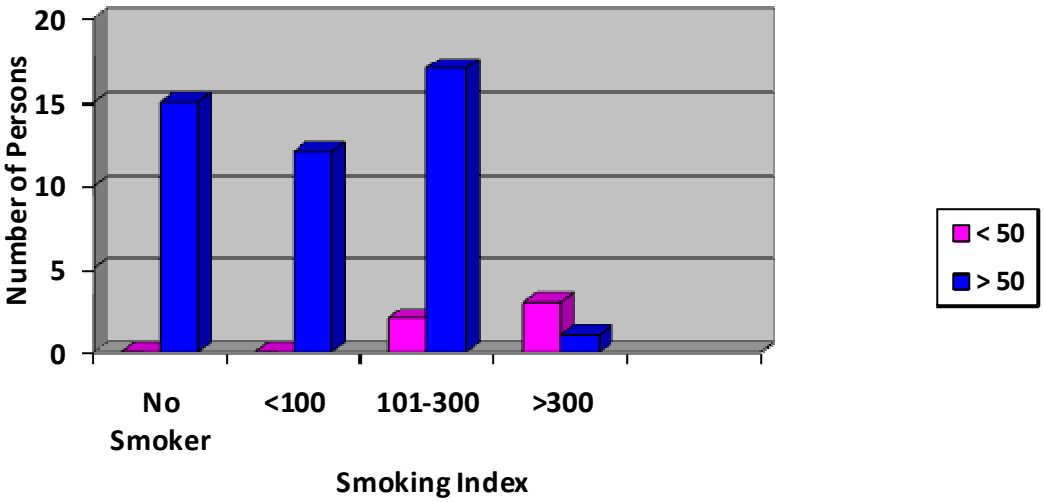
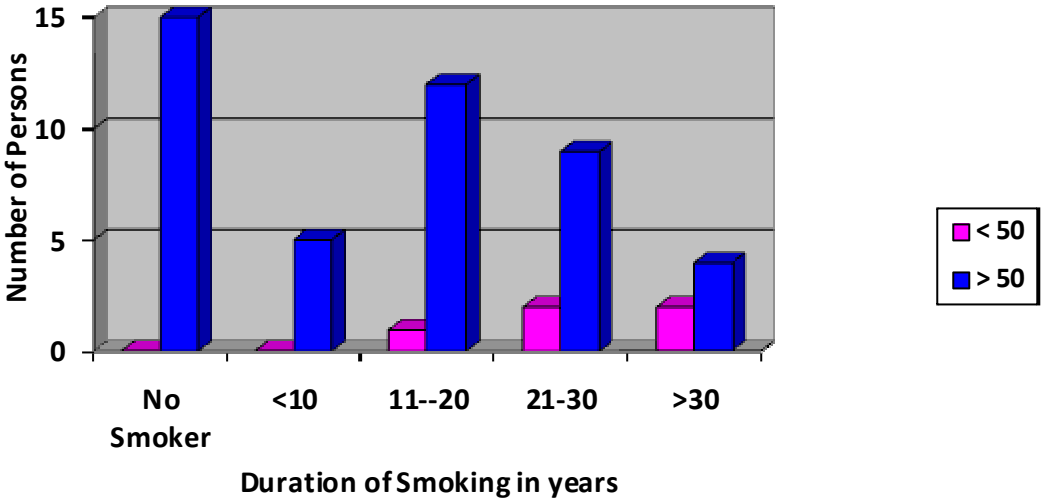


Fig 19: Duration of Smoking and LV Systolic Function



Patients more than 10 years of smoking have LV systolic dysfunction. Patients who smokefor a long duration have higher rates of LV dysfunction.

Table 19:DURATION OF SMOKING AND LV SYSTOLIC FUNCTION

Duration of Smoking in years		Ejection Fraction		Total	p value
		< 50	> 50		
Non smoker	Number of persons	0	15	15	
	% Non-smoker	.0%	100.0%	100.0%	
	% within Ejection Fraction	.0%	33.3%	30.0%	
< 10	Number of persons	0	5	5	
	% within Duration of Smoking in years	.0%	100.0%	100.0%	
	% within Ejection Fraction	.0%	11.1%	10.0%	
11-20	Number of persons	1	12	13	
	% within Duration of Smoking in years	7.7%	92.3%	100.0%	0.01*
	% within Ejection Fraction	20.0%	26.7%	26.0%	
21-30	Number of persons	2	9	11	
	% within Duration of Smoking in years	18.2%	81.8%	100.0%	
	% within Ejection Fraction	40.0%	20.0%	22.0%	
> 30	Number of persons	2	4	6	
	% within Duration of Smoking in years	33.3%	66.7%	100.0%	
	% within Ejection Fraction	40.0%	8.9%	12.0%	
Total	Number of persons	5	45	50	
	% within Duration of Smoking in years	10.0%	90.0%	100.0%	
	% within Ejection Fraction	100.0%	100.0%	100.0%	

'p' value is significant. 33.3% of patients withmore than 30 years of smoking have LV systolic dysfunction. Duration of smoking is inversely related to the LV function.

Table20: SEVERITY OF COPD AND LV SYSTOLIC FUNCTION

Severity of COPD		Ejection Fraction		Total	p value
		< 50	> 50		
Mild	Number of persons	0	6	6	0.001**
	% within Severity of COPD	.0%	100.0%	100.0%	
	% within Ejection Fraction	.0%	13.3%	12.0%	
Moderate	Number of persons	1	34	35	
	% within Severity of COPD	2.9%	97.1%	100.0%	
	% within Ejection Fraction	20.0%	75.6%	70.0%	
Severe	Number of persons	4	5	9	
	% within Severity of COPD	44.4%	55.6%	100.0%	
	% within Ejection Fraction	80.0%	11.1%	18.0%	
Total	Number of persons	5	45	50	
	% within Severity of COPD	10.0%	90.0%	100.0%	
	% within Ejection Fraction	100.0%	100.0%	100.0%	

'p' value is highly significant. In moderate COPD patients only 2.9% of them have

LVEF< 50%. But in severe COPD patients 44.4% of them have LVEF<50%.Among the LV systolic dysfunction patients 80% of them are severe obstructive pattern. Severity of COPD is inversely related to the LV systolic function

Fig20: Severity of COPD and LV Systolic Function

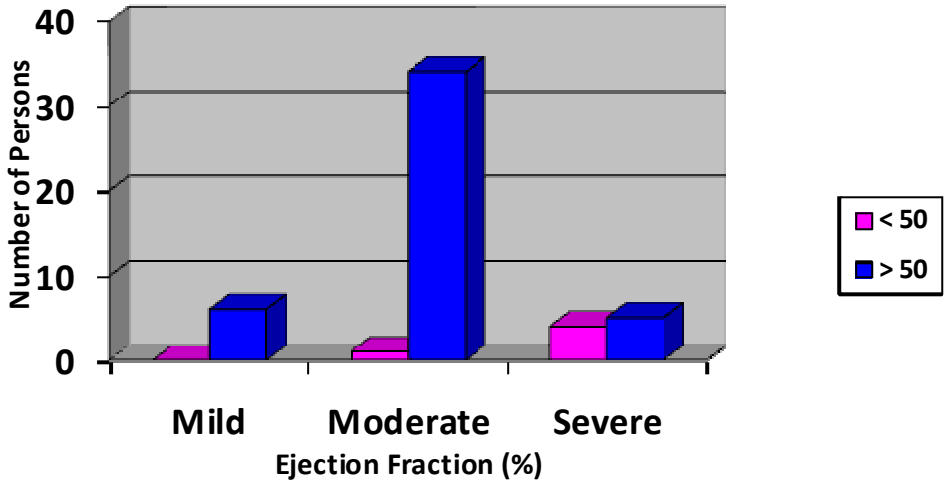


Fig 21: PHT and LV Systolic Function

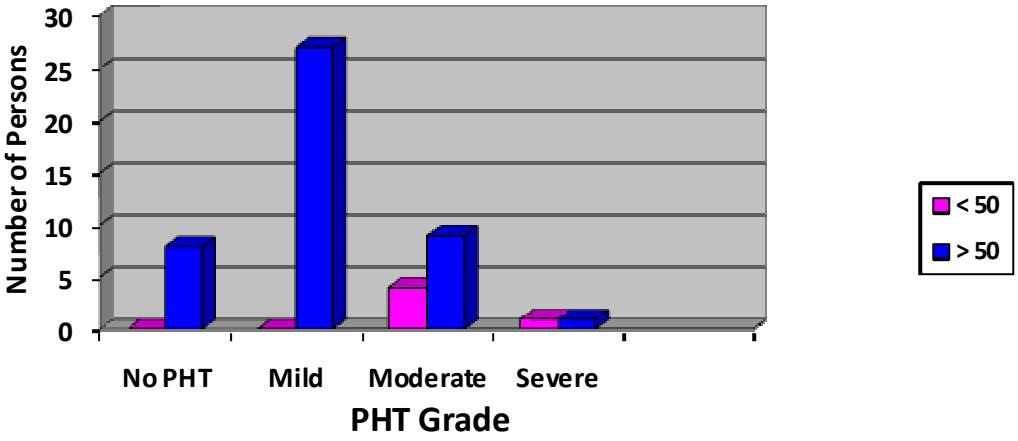


Table 21: PHT AND LV SYSTOLIC FUNCTION

PHT Grade		Ejection Fraction		Total	p value
		< 50	> 50		
No PHT	Number of persons	0	8	8	
	% No PHT	.0%	100.0%	100.0%	
	% within Ejection Fraction	.0%	17.8%	16.0%	
Mild	Number of persons	0	27	27	
	% within PHT Grade	.0%	100.0%	100.0%	0.003**
	% within Ejection Fraction	.0%	60.0%	54.0%	
Moderate	Number of persons	4	9	13	
	% within PHT Grade	30.8%	69.2%	100.0%	
	% within Ejection Fraction	80.0%	20.0%	26.0%	

Severe	Number of persons	1	1	2	
	% within PHT Grade	50.0%	50.0%	100.0%	
	% within Ejection Fraction	20.0%	2.2%	4.0%	
Total	Number of persons	5	45	50	
	% within PHT Grade	10.0%	90.0%	100.0%	
	% within Ejection Fraction	100.0%	100.0%	100.0%	

'p' value is highly significant.

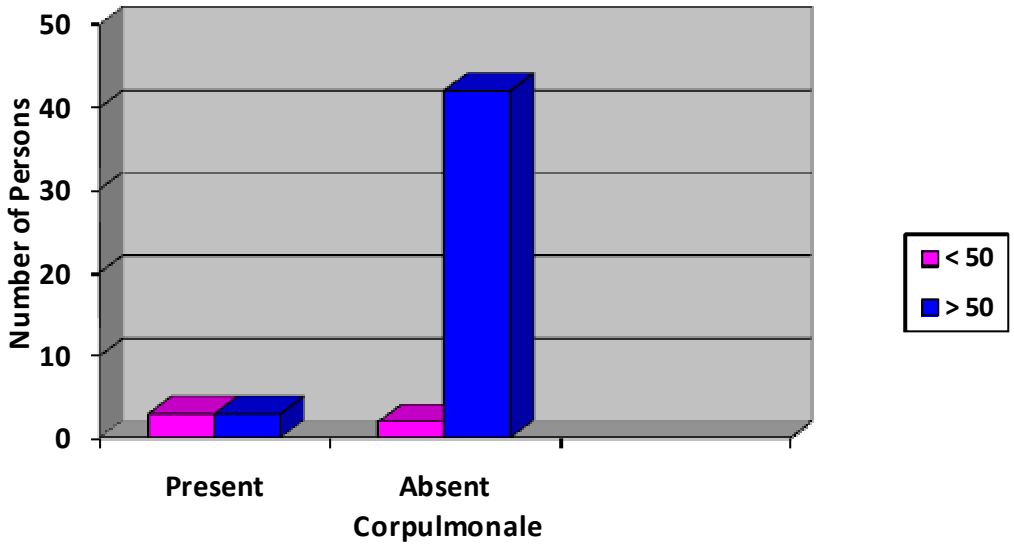
Mild PHT patients have normal LV systolic function. Moderate and severe PHT patients have developed LV systolic dysfunction. In moderate PHT patients 30.8% have LVEF <50%. But in severe PHT patients 50% have LVEF<50%. Severity of PHT is directly related to LV systolic dysfunction.

Table 22: CORPULMONALE AND LV SYSTOLIC FUNCTION

Clinical Features of Corpulmonale		Ejection Fraction		Total	p value
		< 50	> 50		
Present	Number of persons	3	3	6	<0.001**
	% within Clinical Features of Corpulmonale	50.0%	50.0%	100.0%	
	% within Ejection Fraction	60.0%	6.7%	12.0%	
Absent	Number of persons	2	42	44	
	% within Clinical Features	4.5%	95.5%	100.0%	

	of Corpulmonale				
	% within Ejection Fraction	40.0%	93.3%	88.0%	
Total	Number of persons	5	45	50	
	% within Clinical Features of Corpulmonale	10.0%	90.0%	100.0%	
	% within Ejection Fraction	100.0%	100.0%	100.0%	

Fig 22 : Corpulmonale and LV Systolic Function



'p' value is significant. Among patients with clinical features of corpulmonale 50% of them have LVEF<50%.Inpatients without corpulmonale incidence LV systolic dysfunction is 4.5%. This report shows that presence of corpulmonale among COPD patients predicts worsening LV systolic function. 60% of the patients with LVEF<50% have the clinical features of corpulmonale.

DISCUSSION

COPD is now more prevalent in both developed and developing countries. It is a major health burden in the world. According to "WHO "report, COPD at present is the fourth commonest cause of death worldwide.[5] It is projected to be the third most common cause of death and fifth most common cause of chronic disability by the year 2030.In India half a million people die of COPD. [6]This is4 times the mortality that it causes inUSA and Europe.[122]

In our study COPD is more prevalent in males and male to female ratio is 4:1.This is mainly attributed to high prevalence of smoking among males.But according to WHO report thedisease affects men and women equally. In a large, multicentric study from India, the prevalence of COPD among general population was 4.1 per cent and the male to female ratio of 1.56:1.COPD is common in middle aged, so lower age limit of 40 is taken in our study. Most of the COPD patients are between 51 to 60 years of age.As age increases the disease prevalence also increases.This is attributed to age related decline in FEV1.Increasing prevalence with advancing age may reflect either cumulative exposure to smoking

and other risk factors or loss of elasticity of lung tissue or both.National health interview surveyreport in United States in the year 2007 to 2009 shows the prevalence of COPD was higher in older age groups.

Swedish cohort study concluded that smoking was a causative risk factor of COPD with 76.2 percent attributed risk in a given population [27] where as in Denmark study it was 74.6 percent.[28]BTS guidelines reported that most COPD patients have history of at least 20 pack-year of smoking.[21]Nonsmokers commonly have decline the rate FEV1 of about 30mL .Smokers on the other hand have a decline inFEV1 of about50 ml. Our study report shows increasing smoking index increases the prevalence and severity of COPD. 91.7% of mild smokers and 84.2% of moderate smokers belong to moderate COPD. 75% heavy smokers have severe COPD. Our study patients have more than 10 years of smoking have moderate to severe obstruction. In more than 30 years of smoking history, 50% of them have severe obstruction.

Prevalence andseverity is more in low socio economic status. 76% of the COPD patients belongs to low socio economic status due to poor housing condition, overcrowding, poor environment, poor nutrition, alcohol, smoking and recurrent lower respiratory infections.

The development of pulmonary hypertension is a poor prognostic sign in patients with COPD, affecting both mortality and quality of life.Mild-to-moderate pulmonary hypertension is a common complication of COPD. Such a complication is associated with increased risks of exacerbation and decreased survival. Circumstantial and experimental evidence suggests that products of cigarette smoke can initiate pulmonary vascular changes in COPD. Our study reports that 84% of them have pulmonary hypertension. In that 54% of them have mild, 26% moderate and 4% severe PHT. Severity of PHT is more in Moderate and heavy smokers than mild smokers. Duration of smoking is directly proportional to the severity of PHT. Those who are smoking more than 20 years the prevalence of moderate PHT is more. The severity of COPD is directly related to severity of PHT. Severe PHT is present in moderate and severe COPD patients. All corpulmonale patients have severe obstructive pattern and 66.7% of them have moderate pulmonary hypertension.**Smoking index, duration of smoking and severity of COPD are positively correlated with severityof PHT.**

Chronic obstructive pulmonary disease patients have a high prevalence of left ventricular diastolic dysfunction, which is associated with disease severity. Boussuges et al found a high prevalence of left ventricular diastolic dysfunction in COPD patients relative to control subjects (76% *vs.* 35%)Rutten et al[123] and Funk et al also reported a prevalence >50%.[124,125] In our study reports

70% of our patients have diastolic dysfunction. In grade1 diastolic dysfunction patients 71.4% have moderate obstruction and 19.4% have severe obstruction. In grade 2 diastolic dysfunction patients 100% are severe obstruction. **COPD severity worsens the LV diastolic function**. All mild COPD have normal LV function.

LV diastolic dysfunction shows progressive deterioration with increasing severity of PHT. All severe PHT patients have grade 2-3 diastolic dysfunction.

During the period from the first of May 2009 to end of December 2009a group studied theassessment of left ventricular systolic function (LVSF) at Ibn Sina Teaching Hospital wards and respiratory care unit among patients with COPD. The frequency of LVSD among COPD patients were 21.4% and the percentage of LVSD positive patients with pack years > 10 was 100%. These results confirm the association of pack years and mean duration of smoking with development ofLVSD[(95)].Our study reports that 10% of the COPD patients have LV systolic dysfunction. 75% of the heavy smokers and 33.3% of patients more than 30 years of smoking have LV systolic dysfunction. Smoking index and duration of smoking is directly associatedwith the development of LVSD.

A prospective study of 60 COPD patients with or without corpulmonale attending Manipal Teaching Hospital (MTH), Pokhara during 1st March, 2006 to 28th February, 2007 reported the prevalence of LV systolic dysfunction to be found

to be 26.7%. Severe cases 77% and moderate cases 14.2% had LV systolic dysfunction. The findings directly correlate with the severity of COPD i.e., more the severity of COPD more the probability for the incidence of LV systolic dysfunction.[126]In our study only 2.9% of moderate COPD patientsand 44.4% of severe COPD patients have LVEF<50%.Among patients with LV systolic dysfunction 80% showed severe obstructive pattern. Moderate and severe PHT patients have developed LV systolic dysfunction. In moderate PHT patients 30.8% have LVEF <50%. But in severe PHT patients 50% have LVEF<50%.In patients with corpulmonale 50% of them had LVEF<50%.This report shows that, severity of the COPD and PHT is inversely related tothe LV systolic function**. A higher Smoking index, prolonged duration of smoking is associated with poor LV systolic function. Increasing severity of COPD is associated with worsening of LV systolic function.**

THERAPEUTIC IMPLICATION:

Studiesreported that smokingplay an important role in the development of pulmonary vasculopathy; therefore,cessation smoking is avital part of treatment plan in patients with COPD.

Oxygen supplementation can modestly increase exercise tolerance, decrease PVR,PAP and improves the RV function. Long term oxygen therapy (LTOT) is slows and reverses partially the progression of PHT.

Currently, long-acting beta2 adrenoreceptor agonistinhalation is preferred in most COPD patients because it is more quickly removed from myocardial and kidney receptors, thus making potentially deleterious cardiac effects less likely.

Cardiac arrythmias develops if the theophylline in serum levels exceeds 20mg/L. Corticosteroids produce water retention. Hence, these drugs are best avoided in coexistent COPD-HF.

In COPD-HF, metabolic alkalosis occurs due to excessive diuresis that may inhibit ventilation is theoretically but in normal diuretic dosages pulmonary function is not affected.

A recent systematic analysis reported thatcardio selective beta-blocking agents can be safely administered to COPD patients[127].

ACE inhibitors and angiotensin-II antagonist are important for the treatment of HF.It decreases airways obstruction and also prevents the lunginjury. Other benefits are to improve the alveolar membrane gas exchange,decrease pulmonary inflammation and pulmonary vascular constriction.

Aldosterone can damage the alveolar-capillary membrane. Spironolactone has positive effects on gas diffusion.

Digitalis causes pulmonary vasoconstriction and thereforeis not usually recommended in COPD-HF.

In COPD if heart failure is prominent, it may be good to introduce gradually specific beta 1 blocker like Metoprolol or Bisoprolol along with inhalational bronchodilator therapy after optimizing the heart failure therapy with drugs like diuretics,angiotensin converting enzyme inhibitor,angiotensin-IIantagonist and aldosterone antagonist.

CONCLUSION

In our study chronic obstructive pulmonary disease is more common in males. Most patients belong to low socio economic status. COPD severity is directly proportional to smoking index and duration of smoking. Pulmonary hypertension severity is directly proportional to severity of COPD, smoking index and duration of smoking.

LV systolic dysfunction is directly proportional to severity of COPD. Smoking index and duration of smoking are positively correlated with development of LVSD. Our study reports that 44.4% of severe COPD patients have LVSD. So we recommendroutine echocardiography for all severe COPD patients.Smoking cessation should be avital part of treatment plan in COPD patients.COPD obscures the clinical signs of coexisting left ventricular dysfunction like cough, dyspnea, paroxysmal nocturnal dyspnea and orthopnea.Symptoms of dyspnea in COPD can be partially due to LV systolic and diastolic dysfunction. Early identification and treatment of LV dysfunction can improve the patient's symptoms.Routine spirometry is used to diagnose and to assess the severity of COPD and echocardiography is mandatory to assess the cardiac status in COPD patients.

InCOPD patients withLVSD, it may be good to introduce selective beta-1 blocker, diuretics, ACE inhibitors,angiotensin-IIantagonist and aldosterone

antagonist. This treatment improves the LV function,reduces the recurrence ofCOPD exacerbation, improves the quality of life andreduces the morbidity and mortality.

LIMITATIONS:

1. The sample size is small because of the higher prevalence of patients belonging to the diseases mentioned in the exclusion criteria, in the Out/Inpatients population of the place of the study. A larger study in a higher center with more population will be able to predict the true prevalence of LV dysfunction in COPD patients.

2. To rule out ischemic LV dysfunction patients would have required either non invasive nuclear imaging or invasive coronary angiogram. Since the investigations are not available in our hospital we have taken clinical and ECG criteria for CAD.

3.Other rare causes for LV systolic dysfunction such as alcoholic cardiomyopathy are not considered.

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ABBREVIATIONS

COAD—Chronic Obstructive Airways Disease

COPD – Chronic Obstructive Pulmonary Disease.

GOLD –Global initiative for Obstructive Lung Disease

WHO- World Health Organization.

FEV1- Forced Expiratory volume in one second.

FVC-Forced Vital Capacity.

TNF alpha- Tumor Necrosis Factor alpha.

IL-Interleukin.

BTS-British Thoracic Society

ATS-American Thoracic Society

α1-AT-alpha 1-antitrypsin

MMP-Matrix metalloproteinases

BAL-bronchoalveolar lavage

H_2O_2–Hydrogen peroxide

MIP-macrophage inflammatoryprotein

MCP- monocyte chemoattractant protein

CRP-C-reactive protein

TNF-tumour necrosis factor

VEGF-vascular endothelial growth factor

AHR-airway hyperresponsiveness

RV -residual volume

TLC -Total lung capacity

PVR-Pulmonary vascular resistace

RA- Right Atria

RV-Right ventricle

LV-Left ventricle

HF-Heart failure

MAT-Multifocal atrial tachycardia

AF-Atrial fibrillation

PAH-Pulmonary artery hypertension

AVP-Arginine vasopressine

ACE-Angiotensin converting enzyme

ANP-Atrial naturitic peptide

RVH-Right ventricular hypertrophy

BMI-Body mass index

TLCO-Transfer factor for carbon monoxide

KCO- transfer coefficient

PCWP-Pulmonary capillary wedge pressure

BNP-Brain naturetic peptide

LABA- long-acting beta2 agonist

SABA-Shot-acting beta2 agonist

PDE-phosphodiesterase

ICS-inhaled corticosteroid

LTOT-long-term oxygen therapy

LAMA -long-acting muscarinic antagonist

PFT-Pulmonary function test

LVEF-Left ventricular ejection fraction

IHD-Ishemic heart disease

RBBB-Right bundle branch block

LBBB-Left bundle branch block

JVP-Jugular venous pressure

PHT-Pulmonary hypertension

PA-Pulmonary artery

PVAT-PULMONARY VELOCITY ACCELERATION TIME

LVSD-Left ventricular systolic dysfunction

ECG- Electrocardiography.

ECHO- Echocardiography

RAD- Right Axis Deviation

LAD- Left Axis Deviation

NA-Normal axis

TR- Tricuspid Regurgitation

RTI-Respiratory tract infection

PATIENT CONSENT FORM

STUDY DETAIL :
STUDY CENTRE :
PATIENT'S NAME :
PATIENT'S AGE :
IDENTIFICATION NUMBER :

I confirm that I have understood the purpose and procedure of the above study. I have the opportunity to ask questions and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

I understand that the sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However I understand that my identity would not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

I hereby consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic tests including haematological, biochemical, radiological tests.

Signature/thumb impression:

Patient's name and address:

Place: Date:

Signature of the investigator:

Name of the investigator:
Place: Date:

PROFORMA

NAME: **OP / IP No.:**

AGE& SEX:

Occupation:

ADDRESS:

PRESENT HISTORY:

PAST HISTORY:

PERSONAL HISTORY:

GENERAL EXAMINATION

Pallor:	**Icterus:**	**Cyanosis:**
Clubbing:	**Lymphadenopathy:**	**Edema:**
JVP:		
Pulse Rate:	**Blood Pressure:**	**SPO_2:**

CVS:

RS:

P/A:

CNS:

INVESTIGATION

1. **CBC with ESR**
2. **RBS**
3. **Blood glucose –fasting / postprandial**
4. **Lipid profile**
5. **Blood Urea**
6. **Blood Creatinine**
7. **Liver function test**
8. **Ultrasonagram Abdomen**
9. **Chest X-ray**
10. **ECG**
11. **Pulmonary Function test**
12. **Echocardiogram**

SIGNATURE OF INVESTIGATOR SIGNATURE OF GUIDE

DATE

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE, CHENNAI-10

Ref.No.2318/ME-1/Ethics/2012 Dt:04.04.2013

CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "A Study on prevalence of left ventricular systolic dysfunction in chronic obstructive pulmonary disease" – For Project Work submitted by Dr.J.Kamaraj, MD (GM), PG Student, Govt. Royapettah Hospital, Chennai-14.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

29/5/13

CHAIRMAN,
Ethical Committee
Govt.Kilpauk Medical College,Chennai

GOVT. KILPAUK MEDICAL COLLEGE
29 MAY 2013
Kilpauk, Chennai-10.

SL NO.	NAME	AGE (YEARS)	SEX	SMOKING		SOCIO ECONOMIC STATUS	CLINICAL FEATURES OF CORPULMONALE	PFT			ECG					ECHO							
				INDEX	DURATION (YEARS)			FEV1	FEV1/ FVC	SEVERITY OF COPD	P - PULMONALE	RBBB	QRS AXIS	RVH	ECG EVIDENCE OF PHT	RA DILATATION	TR	PA DIA-METER (CM)	PVAT (m sec)	PA PRESSURE (mmHg)	PHT GRADE	DIASTOLIC DYSFUNCTION	EF
1	BABU	57	MALE	60	15	LOW	ABSENT	58%	65%	MODERATE	-	-	NA	-	-	-	MILD	1.5	110	44	MILD	Grade-1	63%
2	PITCHANDI	60	MALE	150	30	LOW	ABSENT	56%	62%	MODERATE	+	+	RAD	+	+	-	TRIVAL	2.9	90	50	MODERATE	Grade-1	65%
3	SUBRAMANI	67	MALE	-	-	MIDDLE	ABSENT	70%	66%	MODERATE	-	+	RAD	-	-	-	MILD	2.2	100	43	MILD	Grade-1	66%
4	MADHAVAN	63	MALE	200	40	MIDDLE	ABSENT	52%	60%	MODERATE	-	+	RAD	-	-	-	MILD	2.3	90	52	MODERATE	Grade-1	56%
5	PARIMALA	60	FEMALE	-	-	LOW	PRESENT	40%	51%	SEVERE	+	+	RAD	+	+	+	MODERATE	2.6	36	58	SEVERE	Grade-2	55%
6	SANTHANAM	64	FEMALE	-	-	LOW	ABSENT	45%	55%	SEVERE	+	-	RAD	-	+	+	MILD	2.3	100	35	MILD	Grade-2	63%
7	SUBBIAH	65	MALE	-	-	MIDDLE	ABSENT	72%	65%	MODERATE	-	-	NA	-	-	-	-	2	130	-	-	Grade-1	61%
8	KUMAR	50	MALE	400	30	LOW	ABSENT	35%	44%	SEVERE	+	+	RAD	+	+	+	MODERATE	2.7	80	53	MODERATE	Grade-1	31%
9	KOWSALYA	45	FEMALE	-	-	MIDDLE	ABSENT	60%	64%	MODERATE	-	-	NA	-	-	-	MILD	2.2	110	48	MILD	Grade-1	70%
10	KABALI	67	MALE	160	40	LOW	ABSENT	55%	63%	MODERATE	-	-	NA	-	-	-	MILD	1.9	100	33	MILD	Grade-1	59%
11	KUPPUSAMY	50	MALE	200	20	LOW	PRESENT	46%	54%	SEVERE	+	+	RAD	-	+	-	-	2.3	110	-	MILD	Grade-1	62%
12	SAKUNTHALA	80	FEMALE	-	-	LOW	ABSENT	56%	64%	MODERATE	-	-	NA	-	-	-	MILD	2.3	120	32	MILD	Grade-1	61%
13	GOPI	60	MALE	200	20	LOW	ABSENT	46%	52%	MODERATE	+	+	RAD	+	+	+	MODERATE	30	56	50	SEVERE	Grade-3	34%
14	SHANMUGAM	60	MALE	300	30	LOW	ABSENT	58%	66%	MODERATE	+	-	RAD	-	+	-	MILD	2.3	100	31	MILD	Grade-1	64%
15	KUPPUSAMY	75	MALE	300	50	LOW	PRESENT	40%	54%	SEVERE	+	-	RAD	+	+	+	MILD	2.8	80	56	MODERATE	Grade-1	65%
16	KAMATCHI	50	FEMALE	-	-	LOW	ABSENT	39%	52%	SEVERE	-	-	NA	-	-	-	MILD	2.2	100	43	MILD	Grade-1	67%
17	DEIVASIGAMANI	75	MALE	400	40	LOW	ABSENT	54%	62%	MODERATE	+	-	RAD	-	+	-	MODERATE	2.6	80	52	MODERATE	Grade-1	61%
18	IYYAPPAN	50	MALE	200	20	LOW	ABSENT	50%	61%	MODERATE	-	-	NA	-	-	-	TRIVAL	2.2	106	32	MILD	NORMAL	65%
19	RANGANATHAN	55	MALE	-	-	MIDDLE	ABSENT	82%	69%	MILD	-	-	NA	-	-	-	-	1.6	126	-	-	NORMAL	68%
20	IYYAPPAN	47	MALE	40	10	LOW	ABSENT	83%	68%	MILD	-	-	NA	-	-	-	-	1.7	130	-	-	NORMAL	67%
21	KANNAPPAN	55	MALE	75	25	LOW	ABSENT	56%	64%	MODERATE	-	-	LAD	-	-	-	MILD	2.5	90	38	MILD	NORMAL	61%
22	PERUMAL	56	MALE	280	28	LOW	ABSENT	58%	62%	MODERATE	+	-	RAD	-	-	+	MILD	2	110	-	MILD	NORMAL	60%
23	BABU	67	MALE	600	40	LOW	PRESENT	46%	55%	SEVERE	+	+	RAD	+	+	+	MODERATE	2.7	73	54	MODERATE	Grade-2	46%
24	ETHURAJ	57	MALE	150	15	LOW	ABSENT	62%	67%	MODERATE	+	+	LAD	-	+	+	MODERATE	2.8	76	60	MODERATE	Grade-1	63%
25	MOHAMEED	74	MALE	200	20	LOW	ABSENT	60%	64%	MODERATE	+	-	NA	-	+	-	MODERATE	2.6	80	56	MODERATE	Grade-1	55%
26	RANI	60	FEMALE	-	-	LOW	ABSENT	80%	67%	MILD	-	-	NA	-	-	-	-	2.3	110	-	MILD	NORMAL	60%
27	KANNIAN	55	MALE	40	10	LOW	ABSENT	56%	61%	MODERATE	-	-	NA	-	-	-	-	1.8	130	-	-	NORMAL	64%
28	CHANDRAN	53	MALE	100	10	LOW	ABSENT	50%	58%	MODERATE	-	-	LAD	-	-	-	-	2.4	110	32	MILD	NORMAL	58%
29	KASINATHAN	63	MALE	200	20	LOW	ABSENT	56%	63%	MODERATE	-	-	LAD	-	-	-	MILD	2.6	100	52	MODERATE	Grade-1	56%
30	ARUMUGAM	59	MALE	-	-	MIDDLE	ABSENT	66%	68%	MODERATE	-	-	NA	-	-	-	TRIVAL	2.3	110	33	MILD	Grade-1	63%
31	RAJENDRAN	45	MALE	-	-	MIDDLE	ABSENT	80%	69%	MILD	-	-	NA	-	-	-	-	1.8	130	-	-	NORMAL	66%
32	KURUVAMMAL	55	FEMALE	-	-	LOW	ABSENT	58%	64%	MODERATE	-	-	NA	-	-	-	TRIVAL	2	110	34	MILD	Grade-1	55%
33	RAJAKANNU	44	MALE	100	10	LOW	ABSENT	54%	58%	MODERATE	+	-	LAD	-	+	-	MILD	2	116	32	MILD	NORMAL	63%
34	KUPPU	50	FEMALE	-	-	LOW	ABSENT	68%	66%	MODERATE	-	+	NA	-	-	-	TRIVAL	2	110	33	MILD	NORMAL	64%
35	VELUSAMY	60	MALE	40	20	MIDDLE	ABSENT	56%	64%	MODERATE	-	-	NA	-	-	-	-	1.8	130	-	-	NORMAL	58%
36	SALIM	65	MALE	90	30	MIDDLE	ABSENT	55%	61%	MODERATE	+	-	RAD	-	+	-	MILD	2	110	34	MILD	Grade-1	60%
37	KRISHNAN	50	MALE	90	15	LOW	ABSENT	60%	66%	MODERATE	-	-	NA	-	-	-	TRIVAL	2.1	110	33	MILD	Grade-1	63%
38	MOHAMEEDKASIM	74	MALE	100	20	LOW	ABSENT	55%	60%	MODERATE	-	-	NA	-	-	-	TRIVAL	2.3	100	33	MILD	Grade-1	58%
39	MARRY	55	FEMALE	-	-	MIDDLE	ABSENT	82%	68%	MILD	-	-	NA	-	-	-	-	1.8	130	-	-	NORMAL	65%
40	RAMASAMY	60	MALE	100	10	MIDDLE	ABSENT	65%	67%	MODERATE	-	-	NA	-	-	-	TRIVAL	2	108	36	MILD	NORMAL	58%
41	NALLAN	65	MALE	300	30	LOW	PRESENT	42%	52%	SEVERE	+	+	NA	+	+	+	MODERATE	2.8	73	52	MODERATE	Grade-1	44%
42	ABDULKADHAR	70	MALE	150	20	LOW	ABSENT	65%	69%	MODERATE	-	-	NA	-	-	-	TRIVAL	2	112	36	MILD	Grade-1	56%
43	RAMALAKSHMI	50	FEMALE	-	-	LOW	ABSENT	83%	67%	MILD	-	-	NA	-	-	-	-	2	130	-	-	NORMAL	64%
44	JAYAKUMAR	60	MALE	150	15	LOW	ABSENT	58%	60%	MODERATE	+	+	RAD	-	+	+	MILD	2.2	110	38	MILD	Grade-1	58%
45	KANNAN	55	MALE	100	20	LOW	ABSENT	60%	64%	MODERATE	-	-	LAD	-	-	-	TRIVAL	2.2	104	33	MILD	Grade-1	57%
46	MURUGAN	65	MALE	120	30	MIDDLE	ABSENT	56%	60%	MODERATE	-	-	LAD	-	-	-	TRIVAL	1.9	112	34	MILD	Grade-1	64%
47	KASIM	58	MALE	200	30	LOW	ABSENT	58%	64%	MODERATE	+	-	NA	-	+	+	MILD	2.6	90	53	MODERATE	Grade-1	55%
48	MEYYAPPAN	65	MALE	120	30	LOW	ABSENT	55%	62%	MODERATE	-	-	NA	-	-	+	MILD	2.3	110	33	MILD	Grade-1	62%
49	ANTONY	70	MALE	350	35	LOW	PRESENT	44%	52%	SEVERE	+	+	RAD	+	+	+	MODERATE	2.7	83	56	MODERATE	Grade-1	48%
50	SANKARAN	60	MALE	250	30	LOW	ABSENT	60%	66%	MODERATE	-	+	NA	-	-	+	MILD	2.9	94	60	MODERATE	Grade-1	58%